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DECLINING FEDERAL HEALTH AND SAFETY STANDARDS: HOSPITAL DISINFECTANTS AND ANTISEPTICS

HEARINGS

BEFORE THE

SUBCOMMITTEE ON
INVESTMENT, JOBS, AND PRICES

OF THE

JOINT ECONOMIC COMMITTEE
CONGRESS OF THE UNITED STATES

NINETY-NINTH CONGRESS

SECOND SESSION

AUGUST 7 AND SEPTEMBER 25, 1986

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DECLINING FEDERAL HEALTH AND SAFETY STANDARDS: HOSPITAL DISINFECTANTS AND ANTISEPTICS

THURSDAY, AUGUST 7, 1986

Congress of the United States,
Subcommittee on Investment, Jobs, and Prices
of the Joint Economic Committee,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:30 a.m., in room SD-342, Dirksen Senate Office Building, Hon. Paul S. Sarbanes (member of the subcommittee) presiding.

Present: Senator Sarbanes and Representative Scheuer.

Also present: William Buechner, professional staff member.

OPENING STATEMENT OF SENATOR SARBANES, PRESIDING

Senator **Sarbanes**. The subcommittee will come to order.

Today, the Subcommittee on Investment, Jobs, and Prices of the Joint Economic Committee holds the fourth in a series of hearings on the current state of Federal health and safety standards, and the social and economic ramifications of lowering them. The subject of today's hearing is hospital disinfectants.

The subcommittee turns to this subject, with its clear implications for the safety and health of the estimated 34 million Americans who will be hospitalized this year, after hearing testimony which leads to concern on the decline in Federal health and safety programs in a range of other areas.

In its previous hearings the subcommittee focused on air transportation safety, on fire prevention and control, and on child health.

This series of hearings was undertaken in response to the growing concern—in the Congress, the press, and the public at large—that the Nation's existing health and safety standards are being undermined by arbitrary and irresponsible budget cuts, in some instances by sweeping deregulation, and often by the complex interplay between the two.

Testimony presented at the hearings has, regrettably, borne out the conclusion of a recent study that "budget cuts, which have been the administration's chief policy weapon toward this end, have fallen most unrelentingly on the relatively new and more vulnerable health and safety agencies."

The study, conducted in 1984 by former EPA Deputy Administrator William Drayton, also concluded that the trend "is not the work of any one manager; it is a governmentwide pattern, with a resulting protection gap potentially enormous in scale."

For the approximately 34 million Americans who will be hospitalized this year, and for doctors and all hospital personnel, the effectiveness and dependability of hospital disinfectants must be a matter of serious concern. Every year, about 2 million Americans come down with secondary—hospital based—infections. The Public Health Service estimates that these infections cause thousands of deaths and contribute to a rising cost in annual health care, estimated at some additional $2.5 billion.

Until 1982, the Federal Government exercised responsibility for assuring the reliability of hospital disinfectants and the products through a testing facility operated by the Environmental Protection Agency in Beltsville, Maryland. Indeed, the Federal Government had assumed that responsibility long before the establishment of the EPA, and the testing program was simply transferred to EPA from the existing pesticide testing program at the Department of Agriculture.

In 1982, however, the administration closed the Beltsville facility and, in so doing, abandoned the Federal role in assuring safe and effective hospital disinfectants. The decision was justified on the grounds it would reduce EPA costs, and that it was consistent with the administration's general policy of deregulation. As far as could be determined, the administration made no effort to weigh the short-term budget savings to EPA against the significantly greater health-care costs over the long term.

Testing of hospital disinfectants today is left to the manufacturers themselves, and to the four States which have their own testing programs and standards. Today's hearing will focus on the adequacy of the current system, both in terms of its ability to assure safe and effective products, and of its cost effectiveness.

We are fortunate to have with us today unusually knowledgeable and experienced witnesses, drawn from several of our major medical schools, from the ranks of those with regulatory responsibilities and from industry, beginning first and foremost with my very distinguished colleague, the junior Senator from Tennessee, Senator Albert Gore, who has made an extraordinary effort not only to define the dimensions of this problem but to develop workable solutions to it.

Senator Gore's efforts on this issue have provided very important leadership in the Congress, and his participation in this hearing constitutes a major contribution to the subcommittee's inquiry.

Before I call on Senator Gore, I'll ask my colleague, Congressman Scheuer, whether he has any opening statement.

OPENING STATEMENT OF REPRESENTATIVE SCHEUER

Representative **Scheuer**. Thank you, Senator. I congratulate you for having shown the leadership for bringing this hearing to the point it is now and I congratulate Senator Gore, my erstwhile colleague, who is sorely missed in the House of Representatives, for his leadership on this issue.

There are few issues that are of more concern to more Americans than their health and controlling their health, and when they become ill they are anxiety ridden enough without the knowledge that millions of them over the course of a year are going to leave a hospital with something that they didn't bring with them to the hospital. They are going to leave with unwanted infections of all kinds: the so-called nosocomial infections that are a blight on our health landscape. We have to get this under control.

I had an operation in the last year at a New York hospital by the chief of surgery, the chief of plastic surgery—this little operation on my cheek. And I noticed he didn't wash his hands. He came in two or three times, fiddled around with my face, and I made a few half-kidding remarks about washing his hands. He said, oh, well, we wash our hands enough around here and he said in passing, if we washed our hands every time we touched a patient, he said, our hands would fall apart.

Well, that troubled me. I think we have to have disinfectants that are clearly safe and that don't damage the patient and don't damage the health care provider, be it physician, nurse, attendant, or whatever.

So this hearing is terribly timely. We are eager to hear what our witnesses say. There is no more important question in the health care field that affects more people than this whole question of diseases that you pick up in hospitals, the so-called nosocomial infections.

I welcome the witnesses and congratulate you again for holding this hearing.

Senator **Sarbanes**. Thank you, Congressman Scheuer. Now we will proceed; first by hearing from Senator Gore—Senator, we'd be honored, if your time permits, to have you join the panel after you finish testifying. We'd be very pleased to have you.

We will then have a panel composed of Mr. Rutala, Ms. Larson, Dr. Gröschel, Dr. Schaffner; and then we will have a second panel with the other four witnesses: Mr. Shaffer, Ms. Rhodes, Mr. McQuade, and Mr. Engel.

With that, we'd be very pleased to hear from you, Senator Gore.

STATEMENT OF HON. ALBERT GORE, JR., A U.S. SENATOR FROM THE STATE OF TENNESSEE

Senator **Gore**. Thank you very much. I, too, want to take this opportunity to congratulate you for your leadership in calling a hearing on this important issue. It's a pleasure to work with you on this issue and to work with my former colleague, Congressman Jim Scheuer. We were chairmen of subcommittees together on the same full committee, and I guess we had more joint hearings than any two subcommittees in the Congress, and we worked very well and effectively together.

I know that both of you have had an interest in this issue and are concerned about the adequacy of Federal monitoring of these vital products used in health care facilities.

Congressman Scheuer referred to nosocomial infections, or hospital-caused infections. It is an extremely serious problem in the American care system. There are some 20,000 deaths each year directly related to hospital-caused infections. And there are many times that number of infections that seriously complicate the illness or injury that the patient originally had in coming to the hospital. And when you calculate the total added costs to America's health care bill, it is a multibillion-dollar addition each year. But the figure that strikes me most powerfully is 20,000 deaths each year.

Now, one of the principal lines of defense against hospital-caused infections is the use, by hospitals, of disinfectants. Now, let me say that clearly, if every single disinfectant on the marketplace worked perfectly and was used in exactly the right manner, there would still be hospital-caused infections and there would still be deaths as a result. But common sense dictates that if a hospital is going to use a disinfectant as one of its first lines of defense against this epidemic of hospital-caused infections, that disinfectant should be reliable. It should work. And if hospitals all across America are using disinfectants that do not work—and, Mr. Chairman, we have found instances where the disinfectants themselves were laced with bacteria, so that the hospital, in trying to prevent hospital infections, was spreading bacteria all across the patient's room, the operating room, et cetera.

Now, obviously there is a national interest in trying to prevent those 20,000 deaths each year, and, in addition, trying to save the many billions of dollars that they cost this country and the pain and suffering they cause the individuals and families involved. And, so, we have had in the past a national effort, modest in scope, to endeavor to ensure the effectiveness of these critical hospital disinfectants.

The last congressional hearings that focused on this particular issue were held more than a decade ago. Since that time, a couple of things have happened. The program that was designed to ensure the effectiveness of these products has been dismantled and the evidence has begun to accumulate that the disinfectants on the marketplace, in many cases, simply do not work, and, as I mentioned, sometimes actually carry the bacteria they are meant to kill.

In 1982, the Federal Government stopped this program and has no plans to continue it. Now, as this subcommittee well knows, the hospitals use these products to clean medical instruments, as well as the operating rooms and patient beds and floors, et cetera. But the latest documents on testing show that more than 20 percent of the disinfectants now in use simply do not work.

The exact number of patients who become victims of infections as a direct result of the failure of these products is impossible to establish. However, there are numerous examples of patients who have become infected as a result of the use of an ineffective disinfectant.

Hospital patients place their lives and well-being in the hands of professionals. If those hands are contaminated as a result of inadequate disinfectants, then obviously the patient pays for the consequences of this potentially fatal disaster.

Now, the laboratory in Beltsville did an excellent job when it was in operation, and the last test results there showed that as many as 72 percent of the disinfectants tested failed in the test for efficacy.

Let me clarify that. At the time of the closing of this lab, the disinfectants chosen for testing were chosen because of some indication that they might be subject to suspicion and, so, the 72 percent rate is a little misleading in that respect. But let me also hasten to add that before they changed their method of selecting disinfectants for testing, previously they used a random selection technique and at that time, the percentage of products failing the test was as high as 30 percent.

Now, at least one State now tests, and we have some random tests from around the country, and we believe the figure is around—is between 20 and 30 percent today.

There are some examples that I would just cite, to illustrate the specific nature of the problem.

Two years ago, doctors at the Mayo Clinic used a bronchoscope to examine the lungs of a tuberculosis victim. They disinfected the instrument using the disinfectant sold for that purpose and following the directions on the label. They subsequently used the bronchoscope on a second patient who did not have the disease, and then a third patient who did not have the disease.

After treating the third patient, they discovered that the disinfectant had failed. I won't go into the details of how this chance discovery had taken place, but the bronchoscope was still carrying the tubercular germs from the first patient and the other two patients had to be treated for months to keep them from developing tuberculosis, and, presumably, if there had not been the chance discovery, in this case, those patients, like thousands and thousands of others, would have come down with a disease that the hospital gave them. And the hospital would have given it to them because they blindly trusted in the efficacy of a product that was sold for the purpose of disinfecting the medical instruments involved.

Now, some people say: Well, why not just leave it up to the hospitals to test. Well, there are so many products on the market and the market is a dynamic, changing market and, interestingly, some documents which I will submit to you will show that the EPA—or the Federal Government—just prior to canceling this program, found that not one single hospital in the United States has a microbiology lab that routinely and continuously tests the disinfectant products that they use. They just can't. It's unrealistic. So this is a legitimate Government role.

Let me give you a second specific. The State of Florida recently found that one of the most commonly used hospital disinfectants, there and around the country, simply does not work. And, in March of this year, the State of Florida ordered the manufacturer, Huntington Laboratories, to stop selling its product, it's called Hi-Tor.

Ironically, the EPA laboratory in Beltsville had found this same product, Hi-Tor, to be completely ineffective in several tests conducted almost 6 years ago. Now, this year the State of Florida has to go back and do that all over again.

Third, the State of North Carolina found bacteria growing inside of the disinfectant sold for the purpose of killing the bacteria. Obviously, using a contaminated disinfectant to fight germs is like trying to put out a fire with gasoline.

Fourth, several companies are—two companies are publicly claiming that their disinfectant kills the AIDS virus, and is effective against AIDS. But the medical community tells us that there is no disinfectant that has been tested as effective against the AIDS virus.

Here again, an example of the kind of false claim in the marketplace that justifies a national effort to prove that these products are effective so that hospitals can rely on them.

Our society simply can't afford to ignore this problem, and closing down the lab was shortsighted and counterproductive. A drop in one of the most useful and cost-effective operations in the Government has cost billions, well, hundreds of millions, perhaps billions, and placed lives in jeopardy.

I have introduced legislation in the Senate to force the Environmental Protection Agency to monitor disinfectants at hospitals, nursing homes, and other health-care facilities once again. Many hospitals are just becoming aware of the problem and will need our help to solve it.

Interestingly enough, Mr. Chairman, the group of manufacturers in this industry that have this organization have joined health-care professionals in calling on the Government to resume testing. I think this is an important point.

Hospitals support resumption of this testing program. Public health professionals support resumption of the program. The industry itself supports resumption of the program. So, what are we arguing about? Who opposes it?

Well, there are two groups of people that oppose it. No. 1, there are a few bad actors in this industry, the ones that consistently sell disinfectants that don't work and place the lives of hospital patients in jeopardy. They don't want testing because they want to be able to continue selling ineffective products, in spite of the fact that they risk the lives of thousands of American hospital patients each year.

The second group that opposes resumption of testing is a small group of ideologues in the administration, who choose to side with the bad actors in this industry and who choose to oppose the responsible industrial participants who want the products tested and who recognize that hospitals cannot assume this burden on their own.

Mr. Chairman, this is the kind of issue that is difficult to get people to focus on and I just want to say very sincerely that I think it's terrific that you would take the time and that you, Congressman Scheuer, would take the time to get involved in an issue that's complicated, complex, and yet can mean so much to the people whose lives can be saved.

In conclusion, I want to offer to you for the hearing record some documentation to support the statement that I have given you. It includes a whole series of EPA documents on this problem, including a list of policy options showing how they analyze the decision to discontinue this testing program. I think you will find that very revealing.

[The documentation follows:]

Memo of July 5, 1983 to Don Clay (Internal EPA Document)

This memo summarizes the EPA position on hospital disinfectant efficacy testing.

p. 2 The failure rate nationwide for all disinfectants is expected to be 20%.

Last page. The failure rates for 1980-82 are 46, 59, and 72 percent respectively. This includes disinfectants that were referred to EPA and suspected of being ineffective.

JUL 5 1983

MORANDUM

: Don R. Clay
Acting Assistant Administrator
Office of Pesticides and Toxic Substances

BJECT: Hospital Disinfectants Efficacy Testing

This is in response to your request that we prepare an ex-anation of the subject issue for possible use at the Adminis-ator's Budget Hearing for OPTS.

Issue

Should EPA test the post-registration efficacy of hospital disinfectants for enforcement surveillance purposes.

Background

A number of factors contribute to the importance of assuring ie efficacy of hospital disinfectants:

--Use patterns are such that they have direct public health significance;

--Market forces cannot be relied upon to control efficacy problems.

--Continuing surveillance is necessary because product failures appear to result from batch-by-batch product variability;

--No private-sector testing or quality assurance program exists which could substitue for public-sector surveillance and testing;

--Because FIFRA subjects hospital disinfectants to FIFRA's registration requirements, the public will assume from EPA's approval of a registration that the product is efficacious. EPA's review of registration data will he assumed to assure some degree of product efficacy whether or not we actively monitor post-registration efficacy.

The Agency's limited experience at post-registration testing evidences a high failure rate among hospital disinfectants. The failure rate for the 500 samples of germicides, sanitizers and hospital disinfectants which EPA has tested since 1978 has averaged over 50%. Of the 80 samples of hospital disinfectants tested in 1980-81, 66% proved to be inefficacious. The samples tested in these early monitoring efforts were selected because their efficacy was brought into question. It is expected that a neutral administrative inspection scheme would reveal a failure rate of up to 20%. This is an unacceptable rate of failure for products with direct public health significance.

In 1968 the USDA was severely criticized by GAO for failing to actively monotor the efficacy of disinfectants and other products found to have a high rate of biological defects. Again in 1974, EPA was criticized by GAO for not conducting an aggressive disinfectants testing program. Then AA for Planning and Management, Alvin L. Alm, indicated that EPA would develop a plan for post-registration testing of disinfectant efficacy.

The mere fact that EPA registers disinfectants encourages the public to assume that they are safe and efficacious. This fact, coupled with the failure-rate data cited above, raises the Agency's obligation to monitor product efficacy and to cancel the registration of patently inefficacious products.

Specific Proposal for Testing the Post-Registration Efficacy of Hospital Disinfectants

CMS proposes to monitor 830 of the 3318 registered hospital disinfectants upon approval of the funding set forth below. Samples would be taken from three different batches of each product, resulting in 2490 routine samples each year. Samples from 5 additional batches would be taken for each of the products shown to be inefficacious by the first set of samples. We anticipate a 20% failure rate. Accordingly an additional 830 follow-up samples would be collected each year, for an annual total of 3320 samples per year for biological testing. This monitoring program would allow sampling of all registered products over a four year cycle.

Each sample would be analyzed for both its chemical content and its biological performance based upon the OPP/CMS protocol developed in 1981. This protocol also sets forth the manner in which both the enforcement program and the registration program will respond with applicable sanctions for inefficacious products (stop sale; administrative penalty; monitoring company QA programs established pursuant to enforcement actions; registration cancellation).

The proposed hospital disinfectant monitoring program would be a cooperative Federal/State program, utilizing where possible the efficiencies of the existing State Grant Program. The program outlined above could be conducted with the following resources:

- --$1.5 M increase in State Grant funds to conduct efficacy testing in sophisticated State labs;
- --5.50 FTEs and $400,000 at NEIC to train State lab personnel, provide QA of State labs, oversee company efficacy programs, and provide a back-up EPA testing capability;
- --1.00 FTEs at HQ to overview and coordinate the national program.

I endorse many of the proposals set forth in Mr. Johnson's June 30 memorandum. These proposals, however, cannot be implemented for a number of years, and will do nothing to fill the void which results from the absence of Federal efficacy testing. The program I have proposed can be implemented immediately and will provide a credible hospital disinfectant compliance program.

In his opening address to EPA staff, Mr. Ruckelshaus told us to behave in every instance as if our actions were placed upon a "billboard" for all to see. The cessation of the efficacy testing program has been the subject of recent Congressional inquiries and newspaper stories and editorials. We should assume that such public scrutiny of our efforts to monitor the efficacy of hospital disinfectants will continue. The program I have proposed constitutes a practical response to what I precieve to be an immediate and significant public health problem.

/s/

A. E. Conroy II, Director
Compliance Monitoring Staff
Office of Pesticides and
Toxic Substances

cc/ Edwin L. Johnson, OPP

Enforcement Response

Phase I

Failure of phase I testing- 2 of 3 batches fail
- Stop Sale of ineffective batches
- Administrative Complaint
- Settelment with Conditions requiring a Quality Assurance Plan be submitted to the Agency

Phase II

Failure of phase II testing- 3 of 5 follow-up batches fail
- Stop Sale of ineffective batches
- Administrative Complaint
- Settelment with Conditions requiring batch testing and submission of data to Agency
- All data forwarded to OPP for appropriate registration action

Program Cost

1.5 Million in state grant money to fund cooperative agreements with states to perform testin

5.5 FTEs and $400,000 at NEIC- positions and funds would be utilized to provide:
a) Quality Assurance of State Laboratories
b) Back-up testing capability to State Laboratories
c) State Training
d) QA and overview of companies doing testing as a result of Phase II enforcement action

1 FTE HQ- position utilized to overview and coordinate national program

Hospital Disinfectant Compliance Program

. Inspection Program

3318 Hospital Disinfectants
25% Products Sampled per Year
3 Batches of each product sampled
2488 Routine samples
829 Follow-up samples taken per year (Samples taken as a result of previous product failures)

3317 Total Samples per year

Testing Program- Based on memorandum of Agreement between A. E. Conroy II and Doug Campt on Public Health related Disinfectant products.

- All samples undergo chemical testing first.
- Biological testing pursuant to A.O.A.C. "Use Dilution Method" (modified for soil load 1-step cleaner disinfectants) for the following organisms:

  a) Salmonella choleraesuis
  b) Staphylecoccus aureus
  c) Pseudomonas aeruginosa

Phase I Testing

- If 2 of 3 batches fail testing, the product will be considered to have failed testing.
- Product that fails phase I testing will result in 5 additional batches of the product being sampled. (Assuming a 20% failure rate, this will reusit in an addition 829 samples being collected or a total of 3317 samples being tested anually.

Phase II Testing

- If 3 of the 5 follow-up batches fail, the product will be considered to have faile phase II testing.

Hospital Type Disinfectants Program

I. Regulated Community

11,698 disinfectants, germicides and santizers registered
3,016 registrants
3,318 hospital type disinfectants registered
1,080 registrants

II. Past Sampling

Year	Number of Samples	Comments
1978	228	germicides, santizers and disinfectants
1979	136	germicides, santizers and disinfectants
1980	111	46% failure rate
1981	40	59% failure rate in hospital disinfectants
1982	40	72% failure rate in hospital disinfectants

Enforcement actions during 1982 - 1 civil complaint
11 stop sales

III. Last Testing

Beltsville Laboratory suspended testing of disinfectants, santizers, sterilizers, and germicides in October 1982

IV. State Jurisidiction

All states have jurisidiction to register pesticides.

Three (3) states have active regulatory enforcement programs to sample and test disinfectants. Actions initiated under state statute.

No testing being done purusant to FIFRA.

Product Performance Information Network for Disinfectants Option Paper, April 1, 1983.

p. 5 the alternatives for EPA are discussed along with the advantages and disadvantages of each. They are:

1. Do Nothing (the current option in use)
   One of the disadvantages is, p. 6 "...product failure may not be detected."

2. Re-Open Beltsville Lab
   This is viewed as, p. 6 "...keyed to buy time..."

3. Do Testing at EPA Cincinnati Lab
   Not viewed as a good alternative.

4. Start Information Network with Sources on Hand
   This would include State labs, universities, etc. but not EPA labs.

5. Contract out Testing
   This would include contracts with commercial labs, non-profit labs, or the States.

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PRODUCT PERFORMANCE INFORMATION NETWORK FOR DISINFECTANTS OPTION PAPER

April 1, 1983
Aram Beloian
Science Support Branch
Benefits and Use Division
Office Pesticide Programs

PRODUCT PERFORMANCE INFORMATION
NETWORK FOR DISINFECTANTS
OPTION PAPER

Introduction

Performance testing of disinfectants in the Office of Pesticide Programs (OPP) is being phased out. This decision was reached on the basis that: (1) there was redundancy in performance testing by the federal government of products registered under the Federal Insecticide, Fungicide and Rodenticide Act after submission by registrants of performance testing data prior to issuance of registration; (2) federal testing of commercial market samples of registered products was infrequent with testing leading to a false sense of security among users as to the efficacy of products; (3) a more active role in surveillance of product performance by users of disinfectants could provide a more effective means for the user community and others to improve their knowledge of deficient products; and, (4) in freeing the laboratory involved from routine testing, more time and effort could be directed at test methods development for greater precision and accuracy of the standardized test method. The goal of this working paper is to identify means for testing performance of disinfectants by establishing information networks among users or testers of antimicrobial pesticides, and to identify options in reaching that goal.

Background

Performance testing of disinfectants (disinfectants used in hospitals and non-medical areas) has been carried out in federal laboratories since the passage of the original Federal Insecticide, Fungicide and Rodenticide Act in 1947. (Prior to that, testing of disinfectants was done under the Insecticide Act of 1910 from 1912 on.) From that time to the present, some testing of disinfectants was carried out after registration of a product. In 1968, the then head of the microbiology group in the Pesticide Registration Division, L.S. Stuart, noted a level of violations from an efficacy standpoint greater than USDA was willing to accept. Beginning in 1969, much more efficacy testing was required by a registrant before registration of a disinfectant was issued (L.S. Stuart, "Testing Sterilizers, Disinfectants, Sanitizers and Bacteriostats" Soap and Chemical Specialities, November 1969). Concurrent with increased test requirements, enforcement sampling and testing of marketed products were increased. The AOAC Use Dilution Test, in use since 1954, is used to determine performance.

Over time the medical community has relied on federal government testing of disinfectants for some assurance that a product will perform. The Center for Disease Control (CDC) has repeatedly recommended to hospital microbiologists not to do performance testing because of lack of expertise and the costs involved. Writing in Manual of Clinical Microbioilogy, 3rd edition, American Society for Microbiology, 1980; Chapter 95, "Sterilization, Disinfection and Antisepsis in the Hospital," page 956, Dr. Martin S. Favero (CDC) wrote: "It is not necessary for hospital laboratories to test the antimicrobial effectiveness of commercial products unless such testing is part of a well-designed research project. Instead, the hospital may rely on the testing performed by the U.S. Environmental Protection Agency for disinfectant agents...Any agent registered with the EPA...may be used with an assurance that the agent meets test criteria for effectiveness. Indeed, testing...of disinfectants is a complex and expensive process and few clinical microbiology laboratories will wish to devote resources to testing that are necessary for reliable results to be obtained."

The consequences of this position among medical experts at CDC and the experience of microbiologists in attempting to conduct performance tests in hospitals, is that hospital and clinical microbiologists are not familiar with AOAC testing, nor do they currently have interest in conducting such tests. Apart from commercial and not-for-profit test labs, who do performance tests for registrants, only three State laboratories – Florida, North Carolina, Virginia – do routine testing of disinfectants. A number of inquiries among major State public health laboratories has confirmed these findings and has shown that such labs only do clinical tests in the same manner as hospitals and do not consider performance testing as a priority item in their work.

BREAKOUT OF VARIOUS SOURCES

LOCAL HOSPITAL INQUIRIES

Walter Reed Army Hospital has no capability to conduct tests. They did not feel that disinfectant testing was a priority item relative to the clinical laboratory work that is priority. They are in the midst of severe staff cuts.

Veterans Administration Hospital, through the head microbiologist, stated that no disinfectant testing has been done. Infection control is practiced by culturing surfaces or articles. The VA hospital may have the capability to do disinfectant testing (night shift), but no firm commitment could be given.

DeWitt Army Hospital (Fort Belvoir) stated that their laboratory is strictly for use as a clinical lab. No capability exists for doing disinfectant testing nor was there any interest in doing future testing.

National Naval Medical Center, Bethesda, stated that their microbiological laboratory is strictly committed to clinical testing. No disinfectant testing capability exists nor have any tests been done in the past. A shortage of microbiologically trained personnel exists for clincal testing; thus, their work load precludes any additional testing.

STATES DOING TEST

Florida, North Carolina, and Virginia do disinfectant testing for enforcement purposes. California and Oregon have expressed some interest, at the State Agricultural department level, to add a test laboratory. There is an unconfirmed report that Georgia is opening a disinfectant test facility (Source: Region 5). Inquiries among EPA regional personnel reveals that the 48 contiguous States include disinfectants under their pesticide statutes. We were unable to determine which of the State statutes were patterned after the FIFRA. This conflicts with information given to us by Enforcement Division.

EPA ENFORCEMENT DIVISION SUPPORT

A meeting was held with John Seitz, John Martin, and David Hannemann, all of the Pesticides Enforcement Division. They stated that no current enforcement grant money to the States covers disinfectants; it only covers analytical chemistry. It was stated that priority enforcement efforts, as identified by OPP, covered such items as the label improvement program and child resistant packaging. They stated that until OPP identifies disinfectant testing in writing as a priority item, Enforcement Division cannot take steps to support this activity with grant enforcement funds, nor could they pass on to OPP any information on performance test violations that are brought to Enforcement's attention. They stated that after the "Cowley decision," in late 1979, they initiated an expansion of the disinfectants enforcement program but as of June 1981 official enforcement efforts for disinfectants ceased. They further stated that any future testing with disinfectants will need to be based on a previous agreement with the Director of Registration Division to cancel ineffective products, rather than continuing registration and batch-testing of production lots.

During the week of March 14-18, the Director of PTSED visited the testing labs in Florida, Virginia, and North Carolina with the professed intent of determining which lab(s) could be relied upon to do 1000 samples per year using federal enforcement funds. It could not be determined if such funding was available or had been approved.

STATE HOSPITAL INSPECTION PROGRAMS

As a possible means to assess the extent of hospital disinfectant testing, State hospital inspection programs are a potential source of information:

Illinois - Department of Public Health, Engineering and Sanitation Division. There are 200 hospitals in Illinois and these are now inspected every 1-2 years. The Division faces cutbacks in personnel.

Indiana - Department of Public Health, Division of Hospital and Institutional Services. There are 120 hospitals in Indiana; they are inspected once a year.

Massachusetts - Department of Public Health, Division of Health Care Quality. Massachusetts has suspended their biennial inspections of hospitals. There are 162 hospitals.

Michigan - Department of Public Health, Health Facilities Services Administration. Hospital inspections are done every 2 years; there are 220 hospitals.

New Jersey - Department of Public Health, Health Facilities Inspections. Hospital inspections are done every year; there are 125 hospitals.

New York - New York Public Health Service, Bureau Hospital Services. Hospitals are inspected once every 2 years; there are 283 hospitals.

All of the above State inspection programs consented to determine if hospitals do disinfectant testing contingent on a formal request from OPP. It would take 2 years to receive results. Moreover, we have been unable to find a single hospital microbiology lab that periodically or routinely does disinfectant testing. Thus, inquiries among hospitals to determine if testing is done appears to be moot.

ALTERNATIVES

Introduction

Five alternatives are discussed in dealing with phasing out OPP testing of antimicrobial pesticides and establishing a user information network that could feed test result information to OPP. The advantages and disadvantages of these alternatives are discussed on the basis of broad inquiries among: affected groups that use disinfectants in medical environments; State agricultural pesticide offices; State public health departments; infection control specialists; EPA Enforcement Division personnel; the American Hospital Association; American Society of Microbiology; selected Departments of Microbiology at universities; Veterans Administration; and the Center for Disease Control, HHS.

A. Alternative 1 - Do Nothing

This alternative proposes that we do nothing overt in seeking alternatives to federal testing of disinfectants. The registrant would provide efficacy data before registration is granted. Users of the registered product who discovered failures of efficacy in actual use situations would publish results in journals. This information would be relayed by BFSD to the Registration Division where action would be taken to reformulate the product or initiate cancellation. (Other options as yet unidentified can be applied here.) It could be made a part of the RS process. Over time, a "network" of users could evolve that could relay test information to OPP as the word went forth that we are now regulating in this new manner.

1. Advantages

   a. This proposed process is consistent with our current emphasis on registration actions.

   b. Failures of products would occur in the "marketplace" and regulatory actions would be based on marketplace (user) findings.

   c. There would be no overt federal intrusion in the marketplace (after registration is granted).

   d. This approach could impel State agencies, individual hospitals and the Center for Disease Control (CDC) to take steps to presumptively assure that disinfectants work.

   e. Registrants, to avoid liability, may be impelled to insist on more rigid testing and greater precision in the test method.

2. Disadvantages

   a. The time lag between a finding of deficiency by a user and publication in the literature would be at least 6-12 months after the deficiency was identified. This may leave us open to criticism. Users may be reluctant to publish results of product failures because of liability suits by patients or restraint of trade suits by registrants.

b. Unless overt cases of infection are noticed among patients by hospital infection control officers, no follow-up testing is performed on a disinfectant; the failure of the disinfectant in this case being only one of several factors that could have contributed to the infection; thus, product failure may not be detected.

c. OPP would be open to criticism from the outside for putting hospital patients in jeopardy based on manufacturer's testing alone. The EPA registration number could become a nullity insofar as medical users are concerned.

d. Registrants may place a disclaimer as to product liability on registered label thus adding to the nullity of federal registration.

B. Alternative 2 - Re-Open Beltsville Lab

This alternative proposes reopening the OPP test lab and continuing testing of marketed disinfectants on a limited basis. This alternative should be considered a temporary measure until such time as testing is initiated on a wider scale outside the federal government than is now the case. This alternative is keyed to buy time; the lab would be phased out by a preannounced date. OPP lab personnel could be used for training outside personnel wishing to start their own testing programs.

1. Advantages

a. Based on over 25 years of CDC recommendations to hospitals not to do their own testing of disinfectants and to have assurance that a product works based on EPA registration, hospitals and CDC would continue present policy.

b. Outside criticism of OPP would abate.

c. State or other labs doing or contemplating doing disinfectant testing would have a key source of expertise to fall back on when testing problems arose.

d. Since routine testing would be limited, more time could be spent on updating existing test methods. [The OPP lab would serve as a key point for initiation of collaborative studies of updated test methods, after new methods are developed through the AOAC in outside labs.]

e. We can buy some time by clearly announcing phasing out of labs so that alternative testing can be initiated outside OPP.

2. Disadvantages

   a. Resources may not be sufficient to sustain laboratory operation.

   b. Reopening lab is not consistent with current emphasis on registration actions and emphasis on restricting federal actions in the marketplace.

   c. The possibility exists that opening the lab will delay opening of alternate test labs at State or other agencies as well as institutions; the alternative may maintain the status quo.

   d. Limited testing of disinfectants could leave us open to criticism for incomplete enforcement efforts.

   e. Registrants would still criticize test methods as needing updating while updating was in progress; this could compromise limited enforcement efforts under this proposal.

C. Alternative 3 - Do Testing At EPA Cincinnati Lab

This alternative proposes to do routine testing of disinfectants at the Microbiology Branch, Toxicology and Microbiology Division of the Health Effects Research Laboratory, Cincinnati, Ohio. The proposal also includes updating standard test methods used for performance testing of disinfectants. Several of the advantages and disadvantages under Alternative 2 apply here as well.

1. Advantages

   a. Testing would still be carried out under the EPA. There would be less opportunity for criticism for external sources of OPP enforcement policies.

   b. Since the Cincinnati lab is oriented to do research, more effort could be given to test method updating thereby mitigating registrant criticism of alleged deficiencies in performance test procedures, while still doing some enforcement.

   c. State and other labs would have a key source of expertise to tap when test problems arose.

2. Disadvantages

   a. Starting lab testing of already registered products for which testing is previously done may be deemed redundant and leading to a false sense of security.

   b. ORD lab personnel are highly reluctant to do routine testing preferring to only do research.

   c. Personnel at Cincinnati have stated that they must have "complete support" to carry out this proposed function. (This means they want funding from OPP.)

   d. Registrants would still criticize test methods as needing updating; this could compromise limited enforcement efforts.

   e. Using an EPA laboratory for testing would stop progress toward de-federalization of regulatory programs and may delay opening of alternate test labs in States or institutions. The marketplace would not be the determining factor of acceptance or rejection of products.

   f. ORD lab personnel could not serve as sources of expertise to other persons wishing to start disinfectant test labs.

D. Alternative 4 - Start Information Network With Sources On Hand

This proposal would have OPP establish performance information networks with all entities that now do disinfectant testing. With hospital disinfectants that would be the States of Florida, North Carolina and Virginia. It would include any research projects such as Dr. William A. Rutala's work with disinfectants efficacy testing for hospital use at the School of Medicine, University of North Carolina. Any registrant who tests a competitor's product and finds a deficiency and submits same to OPP is included. Also, in the food sanitizers field, the State of Wisconsin could be enlisted to provide performance deficiencies of sanitizers used in food processing plants. (Hospital microbiology labs do not do disinfectant testing, per se. Testing is only carried out on medical area surfaces and articles when patients demonstrate hospital acquired infection.) Individual researchers in academia or commercial test labs who do testing for registrants would be reluctant to share deficiency information per se; but, they could be sources of information on test method deficiences. This proposal offers a limited means by which "marketplace" information on disinfectants that fail can be obtained.

1. Advantages

   a. Testing of disinfectant products would be outside the purview of OPP and would be consistent with our current emphasis on registration actions such as registration standards.

   b. This approach would impel more testing at the non-federal level and should expand as it was perceived as doing the job of mitigating or eliminating products that repeatedly fail in the hands of various users. (This would involve development of a standard operating procedure on how to handle received data in the re-registration process.)

   c. There would be no overt federal intrusion in the marketplace after registration was granted.

2. Disadvantages

   a. There would not be wide coverage of the many antibacterial products registered in the limited testing programs identified.

   b. There may be resource problems within OPP in handling incoming data if the number of test labs were to increase from the number available now.

   c. Reports of deficiencies in competitor's products, submitted by registrants, may be open to interpretation because no check testing by an independent source would be done.

   d. No assurance could be given to hospital personnel that the products they use have been independently tested, because of the limited testing that would be carried out.

E. Alternative 5 - OPP Contracts Out Testing

Under this approach, OPP can either contract disinfectant testing to a commercial lab, non-profit lab, or could through interagency agreements have one or more States (already doing their own testing) do testing for us. The legal problems, if any, for this approach have not been identified. Test samples could be sent by users to the test labs. Product samples could also be sent by the Regions, but only at their option. We have 53K in resources for this proposal. Assuming that 70 percent of product samples are hospital disinfectants and 30 percent are sanitizers for food processor use, and based on failure rate of 15 to 20 percent for disinfectants and sanitizers, 250 to 300 samples could be tested per year. (These figures are based on actual commercial lab fees for disinfectant and sanitizer tests and are also based on sampling procedures used in enforcement cases: i.e., for disinfectants, 10 tube test screening; any growth in 10 tubes you test 60-tubes; any growth over 2 tubes is considered failure in 60-tube test.) We could have this testing done solely for use by OPP without going through Enforcement Division as an enforcement case. If we do go through PTSED, they have asked for a memorandum identifying disinfectant testing as a priority item for OPP in FY-83. (As noted on page 6, PTSED is considering using enforcement grant funds to support disinfectant testing at the State level.)

1. Advantages
   a. The approach would be consistent with publicly declared options open to OPP after phasing out testing by OPP.

   b. The proposal would be consistent with professed policy to contract out those federal functions that could be done in the private sector for less cost than in the federal sector.

   c. External criticism of OPP for not doing testing would be mitigated or eliminated. The number of samples tested would exceed the number tested per year when the OPP lab was operating during the last two years.

   d. Test results from a commercial lab would be less apt to be challenged by registrants if that lab also did pre-registration testing for a registrant, when compared to testing done in a federal lab.

   e. Use of a non-profit lab, also used by certain registrants for pre-registration testing, could yield more non-challengeable data than a federal government lab.

   f. Providing resources to State labs could foster opening of other State labs (other than those open now). This would be a temporary incentive. This approach would also foster accumulation of expertise in testing that is much needed at the State level.

   g. OPP would have some performance data that could be used in the re-registration program. (Note: Since RD considers antibacterials as unique formulations, each formulation is required to have substantiating performance data.)

   h. RD would have a means to test performance of sterilizers proposed for registration. In the past, this has always required testing in the OPP lab.

2. Disadvantages

   a. Commercial or non-profit labs accepting a contract to do testing may jeopardize current and future business from test sponsors among registrants or other parties.

   b. Commercial or non-profit labs may be viewed as having a conflict of interest if they carry out testing for OPP, as well as for registrants or other parties. This may leave OPP open to criticism.

   c. State labs that coincidentally test the same product under their enforcement program, as well as under OPP grant may leave OPP open to some criticism for redundant testing.

   d. If testing is done for purposes other than direct enforcement actions, OPP may be open to criticism from user groups (hospitals, CDC, for example).

Recommendations

BFSD proposes to proceed with alternatives 4 and 5. To implement alternative 4, any facility, institution, or individual known or discovered doing peformance testing of disinfectants will be formally approached and requested to become part of a performance information network. Our inquiries among a wide range of medical institutions clearly showed that no disinfectant testing is done because of: (1) budgetary limitations; (2) lack of expertise; (3) strong recommendations from CDC not to do testing and to depend on EPA testing; and (4) no direct knowledge that testing by EPA was suspended. An infection control newsletter (Hospital Infection Control, March, 1983) recently told medical personnel of the suspended testing. What reaction this news will bring cannot be predicted, but it is reasonable to assume there will be some efforts made to initiate testing on a small scale at the largest hospitals. Information from the network could be used in the re-registration program. BFSD proposes to work with RD on how such information can be used directly in the registration program.

To implement alternative 5, BFSD proposes to enter into an interagency agreement with the State of Florida Department of Agriculture and Consumer Services to conduct performance testing of disinfectants. There is $ 53K in resources available in BFSD. The head of the laboratory in Florida has been doing disinfectant testing for the last 10 years and has tentatively agreed to enter into an agreement with OPP.

Implementing alternative 5, together with alternative 4, will buy some time until the user community can be informed if we are to cease all performance testing in the near future, so that alternate user testing could be initiated. Basically, the initiation of such testing among user groups in medical environments would be the Center for Disease Control. BFSD/RD could enter into discussions with CDC on how this could be best accomplished. (The American Hospital Association is not the proper vehicle for this since its main function is accreditation of hospitals.)

Alternative 5 will allow RD to check performance of sterilizers proposed for registration. Our past experience with sterilizers has been that some adjustment nearly always is needed after testing in the OPP lab.

Collection of test samples could be a problem. In the past, EPA regional offices have entered into agreements with State agricultural and public health agencies to collect disinfectant samples for the enforcement program. This part of the enforcement program could be reinstituted. To do this, Enforcement Division will probably ask for a memorandum from the OPP Office Director identifying the activity as a priority item. Failing this, BFSD proposes to contact selected State Agencies with past experience in collecting disinfectant samples for EPA Region Offices and ask them to collect samples as users of disinfectants with OPP doing the testing and sharing the test result information with the State. This proposed approach would set the basis for States cooperatively collecting and testing disinfectants in the future.

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Concur

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Nonconcur

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Date

EPA, Advocacy of Pesticide Uses Which do not Appear on Registered Pesticide Labels; Amendment to the Statement of Policy. May 16, 1986 from the FEDERAL REGISTER May 28, 1986.

This is a proposal for a new policy that would cover the disinfectants for AIDS.

On p. 7 the proposal states, "Recently, data have become available which indicate that HTLV-III/LAV (AIDS virus) may be recovered after drying on inanimate surfaces for extended periods (JAMA, 255:1887-1891, 1986) These findings advance the possibility that the virus may be transmitted via such surfaces."

This is followed on p. 8 "However, since no acceptable protocol has been developed, and no data submitted, no claims have been accepted against AIDS virus for any (disinfectant) product."

6560-50

ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

40 CFR PART 162

[OPP-00149A]

ADVOCACY OF PESTICIDE USES WHICH DO NOT APPEAR ON REGISTERED PESTICIDE LABELS; AMENDMENT TO THE STATEMENT OF POLICY

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of Amendment to Policy.

SUMMARY: This notice amends a policy statement published in the FEDERAL REGISTER of October 22, 1981 (46 FR 51745) (October 1981 policy) and affects persons who distribute, sell, offer for sale, hold for sale, ship, deliver for shipment, or receive and (having so received) deliver or offer to deliver any antimicrobial pesticide. If any such person makes any claims for an antimicrobial pesticide product, targeted against microbial human pathogens, which differ from those made in conjunction with that product's registration, then EPA will regard that person as having violated section 12(a)(1)(B) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), even when such claims are for uses allowed by FIFRA section 2(ee).

DATE: This policy is effective (insert date 30 days after date of publication in the FEDERAL REGISTER).

86P-574

FOR FURTHER INFORMATION CONTACT:

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I. POLICY

FIFRA section 12(a)(1)(B) states that it is unlawful for a person who distributes, sells, offers for sale, holds for sale, ships, delivers for shipment, or receives and (having so received) delivers or offers to deliver a registered pesticide, to make any claims for that product which differ substantially from those claims made in conjunction with that product's registration. The term "claims" includes, but is not limited to, claims appearing in advertising, literature, letters, or other documents, as well as oral statements.

Under section 2(ee) of FIFRA it is not a misuse to:

1. Apply a pesticide at any dosage, concentration, or frequency less than that specified on the labeling.

2. Apply a pesticide against any target pest not specified on the labeling if the application is to the crop, animal, or site specified on the labeling (unless the label states that the pesticide may be used only against pests specified on the label).

3. Employ any method of application not prohibited by the labeling.

In the October 1981 policy, EPA stated its policy that, since a FIFRA section 2(ee) use is not a misuse, any claim made regarding FIFRA section 2(ee) uses would not be treated as a violation of FIFRA section 12(a)(1)(B) unless the registered pesticide's labeling specifically prohibits that use.

EPA has reconsidered its policy on FIFRA section 12(a)(1)(B) with respect to certain claims made for uses not on the labeling. This notice informs the public that a person with financial interest in the use of an antimicrobial pesticide product, targeted against human pathogens, may not make any claims for the product which differ from those on the product's approved labeling. This policy does not affect the applicability of the October 1981 policy to any pesticides other than those specified in this notice.

The Agency believes that efficacy claims for antimicrobial products that are not supported by efficacy data submitted in conjunction with that pesticide's registration may foster a false sense of security among health care professionals relying on that product. Additionally, since the presence of the target microorganism cannot be readily discerned by users, the users cannot easily judge for themselves the effectiveness of that product (see 40 CFR 162.163). Therefore, claims made for antimicrobial products which substantially differ from those made in conjunction with registration could pose a serious public health threat.

Since pesticides intended for use against microorganisms are now excluded from the October 1981 policy, the Agency will take appropriate enforcement action, pursuant to FIFRA, against any person who distributes, sells, offers for sale, holds for sale, ships, delivers for shipment, or receives and (having so received) delivers or offers to deliver any antimicrobial pesticide if any claims made for it as part of its distribution or sale, substantially differ from those made in conjunction with its registration. Additionally, any person who recommends a FIFRA section 2(ee) use for an antimicrobial pesticide remains liable for possible civil damages arising out of his own negligence.

II. BACKGROUND

EPA is currently concerned about unwarranted claims for antimicrobial pesticides used against human pathogens, especially against hepatitis-B virus (HBV), the causative agent of serum hepatitis, and human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV), the apparent etiologic agent for acquired immune deficiency syndrome (AIDS). Most of the inquiries EPA has received concerning control of HBV and HTLV-III/LAV pertain to sterilizer and disinfectant products. Sterilizers are antimicrobial products "...intended to destroy viruses and all living bacteria, fungi and their spores, on inanimate surfaces" (40 CFR 162.3(ff)(2)(i)(D)). Sterilization is an absolute term and denotes killing of all microorganisms, including the most resistant spore forms, against which these products are tested. Disinfectants are antimicrobial products "...intended to destroy or irreversibly inactivate infectious or other undesirable bacteria, pathogenic fungi, or viruses on surfaces or inanimate objects" (40 CFR 162.3 (ff)(2)(i)(A)). In contrast to sterilizers, disinfectants are intended for effectiveness only against representative groups of vegetative bacteria and pathogenic fungi, and against specifically tested viruses. Some antimicrobial products are registered with label directions allowing use as a sterilizer if one treatment regimen is used (e.g., immersion for 10 hours) or as a disinfectant if a less stringent regimen is used (e.g., immersion for 10 minutes).

FIFRA section 3(c)(5)(A) states that the Administrator shall register a pesticide if he determines that "...its composition is such as to warrant the proposed claims for it." In addition, 40 CFR 158.160(b)(1), published in the FEDERAL REGISTER of November 13, 1985 (50 FR 46765), states that efficacy data are required to support all claims "...to control pest microorganisms that pose a threat to human health and whose presence cannot be readily observed by the user, including but not limited to, microorganisms infectious to man in any area of the inanimate environment." EPA requires the following data prior to registering a product with a virucidal label claim: (1) demonstrated recovery of the infective form of the particular virus dried on an inanimate surface, and (2) availability and use of suitable assay methods to demonstrate absence of the dried virus after treatment of the surface with the antimicrobial product (Pesticide Assessment Guidelines, Subdivision G - Product Performance, Section 91-30 (d)(5), National Technical Information Service Order Number PB 83-153924).

To register a product with a label claim that the product can be used as a sterilizer, EPA requires data showing that the product is sporicidal. (Pesticide Assessment Guidelines, as above, Section 91-30(a)(1)). Since spores are the most resistant form of microorganism, no additional data are needed to support virucidal claims for products that are already registered as sterilizers. While HBV is a relatively well understood human pathogen, there are only limited experimental data concerning viral recovery and inactivation by disinfectants on hard surfaces. This is due to lack of a suitable assay method for determining whether the infective virus remains on hard surfaces after disinfection. To determine this, the experimenter must attempt to grow the virus in a host system.

The only known nonhuman host system is the chimpanzee, and chimpanzees are practically unavailable for such experiments. In 1983 the Centers for Disease Control (CDC) published findings of a clinical study in which five chimpanzees were injected with dried HBV-infected plasma treated with each of five different germicides (J. Clinical Microbiology, 18(3): 535-538, 1983). Though the chimpanzees did not show evidence of HBV infection after 9 months, these data are too limited to be conclusive. Therefore, the data are inadequate to demonstrate that disinfection provides adequate control against HBV contamination when sterilization may be the only effective control measure. This discrepancy in control procedures (i.e. disinfection rather than sterilization) could result in failure to reduce HBV contamination, thereby increasing public health risks.

The only known routes of transmission for AIDS virus, which was isolated and identified in 1984, are through sexual contact, blood products, or from mother to newborn. Transmission of AIDS via casual contact has not been demonstrated (New England Journal of Medicine, 314(6):344-349, 1986). Recently, data have become available which indicate that HTLV-III/LAV may be recovered after drying on inanimate surfaces for extended periods (Journal of the American Medical Association, 255:1887-1891, 1986). These findings advance the possibility that the virus may be transmitted via such surfaces. Given the insidious and fatal nature of AIDS, hospitals and other health-care facilities are seeking guidance on the effectiveness of antimicrobial chemicals in controlling the spread of HTLV-III/LAV. Researchers at both CDC (J. Infectious Diseases, 152(2):400-403, 1985) and the Pasteur Institute (Lancet, 2:899-901, 1984) have conducted studies demonstrating that certain chemicals effectively kill HTLV-III/LAV in liquid suspensions. The CDC issued a report to advise interested parties of their recommendations for preventing transmission of HTLV-III/LAV in the workplace (Morbidity and Mortality Weekly Report: 34(45):681-695, November 15, 1985). The report emphasizes that the recommendations for preventing transmission of AIDS are directed towards people who may be exposed to blood or body fluids from persons who may be infected with HTLV-III/LAV. The report provides certain broad recommendations for sterilizing or disinfecting inanimate surfaces or objects that have been in contact with blood or other body fluids of an AIDS patient.

If HTLV-III/LAV can be recovered from inanimate surfaces, it appears that an acceptable protocol can be developed to test the efficacy of antimicrobial products (Journal of Immunological Methods 76:171-183, 1985). However, since no acceptable protocol has been developed, and no data submitted, no claims have been accepted against AIDS virus for any product.

III. SUMMARY

Given the available evidence and methodology concerning these viruses, EPA lacks sufficient basis to approve HBV or HTLV-III/LAV virucidal claims for any disinfectant product. This situation may change as research on the AIDS and HBV viruses continues and registrants develop acceptable protocols to demonstrate virus isolation and disinfectant product efficacy.

EPA will allow registrants to make HBV and HTLV-III/LAV virucidal claims for sterilizer products when used in accordance with label directions for the sterilization procedure, and when approved in connection with the specific product registration.

Dated: MAY 16 1986

Assistant Administrator
for Pesticides and
Toxic Substances.

Senator **Sarbanes**. Thank you very much, Senator Gore, for a very powerful statement and also for the really fine work you have been doing on this issue. I share your very deep concern about it.

I want to note one point I think is very important. The current arrangement is of benefit only to the irresponsible manufacturer, the one who is not prepared to meet adequate standards. And, in fact, the current arrangement is dragging down the responsible manufacturers toward the lowest common denominator. If we had an effective testing program which effectively screened out irresponsible manufacturers, it would be not only to the advantage of health care but to the advantage of people in the industry who are trying to conduct themselves in a proper fashion. There are a number of good actors in the industry, but they risk being discredited by the bad actors. Like you, I don't see where this testing function can be put, where it can be carried out effectively, except by the Federal Government.

At the time the lab was closed in Beltsville, the argument was made: The States can do it. But only a handful of States have done it. Their jurisdiction is only within their State boundaries in any event, whereas the economy is a national economy, the manufacturers function on a national basis. It's ridiculous—at least in my view—to expect the hospitals and the nursing homes to undertake, each of them, a testing program for disinfectants. It is not the kind of issue where you can say: Let the product onto the market. If it doesn't work then people will stop using it. The only way we discover that it doesn't work is when people get sick and perhaps even die. So you haven't tested it until you have suffered these disastrous consequences.

Senator **Gore**. Mr. Chairman, if I may interject, at that point, even then you are likely not to know that the death was the result of the ineffective disinfectant. Because in many cases the infection takes place and—I tried to think of a quick one-liner to cover that but I couldn't think of one, Mr. Chairman—but in many cases the disinfectant will fail, the infection takes place, and nobody knows exactly why that infection took place. There are numerous examples of patients going into the hospital for routine procedures, they stay there for a couple of days, the procedure is over with, all of a sudden they come down with something else. They say to the doctor: I felt good when I came in. What is this? The doctor says: I don't know. I don't know. You have come down with something. It's probably something you got before you came in the hospital and—or, we don't know. We just don't know what has caused it.

That's the typical scenario. And yet, statistical studies prove that they are being caused in the hospitals themselves.

But your basic point is absolutely correct. The marketplace is not going to solve it. It's not going to be solved unless there's a Federal program to deal with it.

Senator **Sarbanes**. Congressman Scheuer.

Representative **Scheuer**. Thank you, Mr. Chairman. I appreciate your testimony very much, Senator. Would the Food and Drug Administration have jurisdiction here?

Senator **Gore**. Well, no. Because this comes under FIFRA. Because of the nature involved, disinfectants——

Representative **Scheuer**. Has there been any study——

Senator **Gore**. Antiseptics come under the jurisdiction of FDA, but disinfectants do not.

Excuse me. Go ahead.

Representative **Scheuer**. Might it be an easier legislative path to amend the FDA legislative jurisdictional coverage by including disinfectants along with antiseptics, because they have the long-time expertise in testing of all kinds, which I would think is somewhat strange to EPA.

Senator **Gore**. That's an interesting suggestion, and one which I think should be explored. But the traditional jurisdictional division has been that FDA covers things that are applied to the skin, that are used in treatment of the patient, ingested by the patient or whatever. And when you have a product that is applied to a chair or a floor, that comes under a different legislative framework. And I think that FIFRA can be amended, and I think that it may be that we can go that route easier than FDA, but your suggestion is a novel one which I think should be considered.

Representative **Scheuer**. Going off the record for a moment.

[Discussion off the record.]

Representative **Scheuer**. Going back on the record. Have there been any studies on the whole question of nosocomial infections in the hospitals, as to whether it's hospital negligence in applying, let's say any disinfectant, or is it the problem of their applying diligently and scrupulously a disinfectant that doesn't work?

Senator **Gore**. I'm going to suggest, only partly out of modesty, that you defer that question for the excellent expert witnesses who will follow, one of whom, Dr. Bill Schaffner, is from my home State and in my opinion the leading expert on this subject in the country. But there are many others who can answer those kinds of questions with far more authority than I can.

Representative **Scheuer**. Very good. Let me just ask you one more question and you may give me the same answer. What has been the experience of other developed countries—England, France, Germany, Switzerland, and the Netherlands—the Scandinavian countries, Australia, New Zealand, Canada, and Israel?

Senator **Gore**. Both England and the Scandinavian countries——

Representative **Scheuer**. Do they have a lesser level of nosocomial infections than we do and if so, why?

Senator **Gore**. I believe they do, but in any case the experts can elaborate on that. I do know that they do a much better job of testing. And the results of that testing you can get from the experts. But I believe that they have a better record.

Representative **Scheuer**. Well, I congratulate you for your initiative in this matter. It's a terribly important one that has been neglected, not only by the administration but frankly by the Congress, too, and you have taken a very important leadership role there and it's very much to your credit.

Senator **Gore**. Thank you very much.

Senator **Sarbanes**. Thank you, Senator Gore. If your time permits and you want to join the panel, we'd be happy to have you. I know you have other pressures on your schedule.

Next, we'll have our first panel, which will consist of Mr. William Rutala, research associate professor from the University of North Carolina School of Medicine; Ms. Elaine Larson, professor of the School of Nursing at Johns Hopkins University; Dr. Dieter Gröschel, professor of pathology and internal medicine, the University of Virginia Medical Center; and Dr. William Schaffner, professor and chairman of the Department of Preventive Medicine at the Vanderbilt Medical School.

This is a very distinguished panel. We are very pleased to have you with us this morning. I think we'll begin with you, Dr. Schaffner, and then just proceed across the table in the order in which you are sitting.

STATEMENT OF WILLIAM SCHAFFNER, M.D., PROFESSOR AND CHAIRMAN, DEPARTMENT OF PREVENTIVE MEDICINE, VANDERBILT MEDICAL SCHOOL

Dr. **Schaffner**. Good morning, Mr. Chairman, Congressman Scheuer and Senator Gore from Tennessee. My name is Dr. William Schaffner and I am professor and chairman of the Department of Preventive Medicine and also chief of the Division of Infectious Diseases of the Department of Medicine at the Vanderbilt University School of Medicine in Nashville. Since 1969 I have chaired the infection control committee of the Vanderbilt University Hospital, and also during this time I have been active in a number of scholarly and professional organizations concerned with hospital infection control. Thus, I come to you with a long standing interest in this area.

Perhaps we might begin by putting this matter into perspective. That's an awfully illuminated screen, but let's see if we can just—if these slides will show up.

[Slide.]

I wanted to show you. This is somewhat removed from the halls of the Senate, but I wanted to remind everyone what we are talking about. This is a baby who just had cardiac surgery and is in the surgical intensive care unit at Vanderbilt University Hospital and you can begin to appreciate the impact of high technology in medical care in this little baby.

[Slide.]

This is another infant in the neonatal intensive care unit at our institution, fragile, in the so-called isolette or incubator.

This is a baby, smaller.

[Slide.]

Some of these babies survive. This is a baby whom I can hold in the palm of my hand.

[Slide.]

Clearly, hospital-acquired infections have long been recognized as a serious problem. Today, hospitals have the capacity and have been demonstrated to provide extraordinarily complex care to gravely ill patients. Even when carried out meticulously, however, certain diagnostic and therapeutic procedures are associated with the risk of complicating infection.

In general, approximately 5 percent of patients admitted to hospitals in the United States acquire an infection during their stay in the hospital. Among the more seriously ill, for example, those cared for in an intensive care unit, or patients with leukemia, the risk of infection is higher, and, it should be noted, that as our population ages and as medical science continues to produce even more dramatic diagnostic and therapeutic innovations, the population of patients in our hospitals at high risk of acquiring an infection is likely to increase.

In order to keep the risk of hospital-acquired infections to a minimum, every hospital has an active and practicing infection control committee. These committees have as their goal the provision of an environment for patients which is as safe as possible, and therefore they have wide-ranging responsibilities. They establish infection control procedures for every area of the hospital, they conduct the surveillance activities which document the occurrence of hospital-acquired infections, they undertake investigations of unusual problems which may arise, and they influence policies in all areas of the hospital: the employee health service, inpatient care practices, and even policies regulating the visiting of patients by friends and family.

These committees can now draw upon a large body of scientific information which has accumulated over the last 20 years, and, as has been stated, an essential feature of every hospital infection control program is the appropriate use of disinfectants and antiseptics.

An elementary, but still extremely effective, way to interrupt the transmission of bacteria and other infectious agents in the hospital is by carefully washing the hands after every patient contact. Clearly we rely upon antiseptics to help us do this job properly.

Every time a patient has an operation or has a diagnostic procedure, or has an intravenous line placed, or has a catheter inserted, et cetera, et cetera, antiseptics are used to disinfect the skin.

Likewise, we employ disinfecting agents to cleanse the hospital's inanimate environment of potentially infecting agents. Here the most critical areas are in the intensive care units. Also included are the various instruments which have direct contact with the patient, both outside and inside the patient's body.

Once again, it is clear that hospitals must rely upon the action of disinfectants in order that these aspects of the environment be rendered free of an infection hazard. Thus, you can see that hospitals use antiseptics and disinfectants constantly and that these agents are critical to the infection control program.

As you've heard, antiseptics and disinfectants are available in a wide variety of formulations and from a large array of manufacturers. I wish it were not so, but it is a bewildering and sometimes frustrating exercise for those of us in infection control to assist our hospitals in selecting the products which are best suited to our various needs.

We are sometimes faced with a cacophony of claims from manufacturers. Infection control practitioners look to the Federal Government for certification of claims of product integrity, substantiation of claims of product effectiveness, and advice on how the products are to be used most efficiently. Unfortunately, under the current, complex, "nonsystem," I would call it, little support or advice is available.

You are aware, I'm sure, of the roles which major Federal agencies—the Environmental Protection Agency, Food and Drug Administration, and the Centers for Disease Control—may or rather, currently do not, play in this area. Therefore, I should like to make a few observations from the front lines of hospital infection control.

First, it may surprise you to hear that, despite my long involvement with infection control, I do not consider myself qualified to make truly insightful judgments about the many available disinfectants and antiseptics. I am quite knowledgeable concerning many aspects of infection control—epidemiological, administrative, clinical—but I'm not a chemist. Some of my colleagues, Ms. Larson and Mr. Rutala here, are experts in this area, but I believe I'm representative of the majority of physicians and nurses who devote themselves to infection control, but who are not sophisticated about antiseptics and disinfectants. We are in need of both relevant data and good advice.

Second, as Dr. Gröschel will state very clearly and as Senator Gore has mentioned already, the clinical microbiological laboratories in our hospitals do not have the equipment, the expertise, the time, or the funds to undertake the analyses necessary to evaluate disinfectants and antiseptic products.

Third, what I know of the microbiological tests of efficacy that are currently required for licensure or registration of antiseptics and disinfectants has left me with the impression that they are not as germane to the current needs of hospitals as they ought to be.

Specifically, while the test organisms in current use do have some utility, they are limited and do not address many of the hospital infection problems we face today. We are coping with bacterial strains which are resistant to multiple antibiotics. I should like to see representative examples—maybe include multiresistant Serratia, Enterobacter, Pseudomonas, Staphylococcus aureus, and the like—included in the panel of test organisms.

Furthermore, the most frequent test questions that I encounter concern two viruses: hepatitis B, and the human immunodeficiency virus, the virus associated with AIDS. From my perspective, the EPA and the FDA seem to be ignoring these vital issues. In the meantime, we in the hospitals are taking care of patients with these diseases and we cannot ignore the issues. We need some guidance.

Fourth, the detection of an increase in the number of infections resulting from either an ineffective degerming product, or one which has become intrinsically contaminated, is often very difficult.

As Senator Gore has said, the increase in infections may be subtle and its recognition by our surveillance methods may be notably delayed. Therefore, as with drugs, assuring the quality of a product before it is sold is imperative. To promote the correct use of the product, its labeling on the container, on the carton, and in the accompanying literature must be clear, correct, and consistent. This is not always the case at the present.

Last, a word about communication. Hospitals are very busy places, and infection control units have many duties. Therefore, the communication of information to hospitals about the safety, efficacy, acceptability, and proper use of disinfectants and antiseptics must be clear and must be couched in terms that can be easily understood. That requires that people in the Federal agencies be deeply knowledgeable about hospitals, about the infections which occur, the diseases patients have which render them susceptible to certain infections, infection control committees, how they work, and the like. Again, from my perspective, neither the EPA nor the FDA currently has such talent on board.

Note, I would like to make it clear that I acknowledge the expertise of their personnel at the laboratory bench. Those good folks, however, do not have the background to communicate effectively with hospitals.

Fortunately, the CDC, with its Hospital Infections Program and other specialty areas, has this expertise. The CDC is held in very high regard by infection control personnel and has repeatedly demonstrated its capacity to communicate quite effectively with hospitals. The channel of communication between hospitals and the Centers for Disease Control is open in both directions.

I suggest that we need some sort of interagency arrangement between the EPA, FDA, and CDC that would provide CDC all relevant data so that it can issue periodic advisories concerning disinfectants and antiseptics. Of course, the CDC would require appropriate legal and administrative safeguards so it could perform this function without undue interference. Unfortunately they no longer feel comfortable in discussing antiseptic and disinfectant issues, so this former source of guidance has recently been silenced.

It goes without saying that an appropriate staff at the Center would be required, if it again were to undertake such a role.

Our current problems with hospital disinfectants and antiseptics are serious and complex. We in the infection control community are both pleased and grateful that you are devoting your time and interest to these issues. Our patients are grateful also. Thank you very much.

Senator **Sarbanes**. Thank you, Dr. Schaffner, for a very helpful statement. We'll proceed through the panel and then direct our questions to the panel in its entirety. So, Dr. Dieter Gröschel, M.D., professor of pathology and internal medicine.

STATEMENT OF DIETER H.M. GRÖSCHEL, M.D., PROFESSOR OF PATHOLOGY AND INTERNAL MEDICINE, UNIVERSITY OF VIRGINIA MEDICAL CENTER

Dr. **Gröschel**. My name is Dieter Gröschel and I'm the chairman of the Committee on Laboratory Practices for Microbiology of the Public and Scientific Affairs Board of the American Society for Microbiology. The ASM is pleased to have this opportunity to comment on the registration of chemical disinfectants and sterilizers for use in health-care institutions.

The majority of its 34,000 members is engaged in health-related work. Many are clinical microbiologists, infectious diseases specialists, and hospital epidemiologists.

In February 1983, we learned that the Office of Pesticide Programs of the Environmental Protection Agency had ceased operation of its testing laboratories for disinfectant efficacy without public knowledge. Concerned by the sudden change in policy, I informed my colleagues by writing an editorial for the journal Infection Control which questioned the wisdom of closing the laboratory. The ASM expressed its concerns to Mr. William Ruckelshaus, then

EPA Administrator, in July 1983, and requested information about the termination of the inhouse testing program without public notice or explanation, and about proposed alternatives to this program. The letter stressed the importance of the EPA registration and label review for safe-guarding public health.

EPA's response listed, among other reasons, that the laboratory, in previous years, had screened samples only infrequently and that the approved laboratory tests had to be revised. The EPA letter stated also that by "having removed the 'security blanket' of federal disinfectant testing, * * * private sector groups * * * would have an interest in undertaking a credible testing program. But, to date, little interest has been demonstrated. Though cognizant of the problem, hospitals do not appear to have adequate resources or the inclination to become involved."

We agree with the EPA that hospital laboratories do not have the expertise and resources, due in part to the fiscal constraints from TEFRA and DRG legislation, to assume local testing. Nor do the 46 or 47 States without disinfectant testing facilities have the resources or the capabilities to establish their own preregistration and enforcement testing programs according to FIFRA.

It appeared to ASM that EPA was simply trying to find a reason to remove the testing laboratory activities from its budget, and, therefore, ASM requested in October 1983 a more detailed and scientific answer from EPA. Copies of this correspondence were provided to several Members of Congress, including Senator Sarbanes. In response, Mr. Ruckelshaus invited ASM to meet with the new Assistant Administrator for the Office of Pesticides and Toxic Substances, Dr. Moore.

During a meeting in January 1984, EPA listed the reasons for termination of the disinfectant efficacy testing, as it was outlined in several of our presentations, and also affirmed the interest of EPA to improve existing methodology for official testing, and to design a scheme for testing, monitoring and enforcement that is economic as well as effective.

After some discussion, Dr. Moore asked if ASM would be willing to explore with EPA the design of a program, possibly by contracting out. ASM agreed in principle to participate, but only as one of several scientific organizations, and that actions would be required on several levels, including manufacturers and local and State agencies. Since then, ASM has been planning with other organizations a national symposium to discuss in detail the present status and the future needs for testing and registering chemical disinfectants and sterilizers in the health care field.

The reason we are concerned about the closure of the EPA Office of Pesticides' testing laboratory in 1982 is our worry about the Federal Government's plans to assure the public that EPA-registered germicides are safe and effective, as claimed on the labels. We discussed with our colleagues the responsibility of the Federal Government to the public and the reasons for removing the Federal "security blanket" in the field of disinfection and sterilization.

As consultants to our institutions, we are responsible for disinfection and sterilization in hospitals, operating rooms, nurseries, intensive care units, et cetera, and EPA's action has placed us and our patients at risk. We cannot understand how a Federal agency charged by law to ensure efficacy and to enforce regulations can abrogate its responsibility by making the user finally responsible.

I would like to give you two examples from the recent literature as justification of our concerns.

One is the famous case of the Serratia marcescens outbreak in Florida complicating cardiopulmonary operations, traced to a disinfectant contaminated with this organism which was reported by Ehrenkranz and collaborators in "Lancet" in December 1980. The other report concerned the failure of a chemical disinfectant to prevent the transmission of Salmonella newport through a sigmoidoscope that had been used on a patient infected during a food-borne outbreak in the Midwest, reported by Holmberg and collaborators in the New England Journal of Medicine in 1984. Both disinfectants were EPA-registered for use with related bacteria. As with all nosocomial infections, the patients pay the bill.

We believe that the Federal Government should show leadership in reviewing and updating official test methods. Recently, EPA published a policy on testing methods in the Federal Register, stating that a new quantitative test methodology for tuberculocides—developed by a manufacturer who is going to testify later—is acceptable, but that the old AOAC method is still accepted for registration, if either modified as to time and/or temperature of testing, or, in the case of glutaraldehyde-based and quaternary ammonium compounds, is supported by validation data from a second testing facility. Many professionals in the field believe the second testing facility should be a governmental laboratory, preferably at the EPA.

Now I would like to just point to an area Congressman Scheuer testified on earlier. We are concerned that there are two different Federal agencies involved in the regulation and testing of chemical germicides: FDA and EPA. The FDA is charged by law to approve antiseptics, as pointed out by Senator Gore, and EPA registers chemical disinfectants and sterilizers. However, if a disinfectant is used to decontaminate a medical device, test results submitted by a manufacturer are reviewed and approved by the FDA as an accessory to a device. On June 27 this year, the issue of the Centers for Disease Control's "Morbidity and Mortality Weekly Report" stated that the bacterial contamination of a device-disinfecting agent, approved by FDA for decontaminating hemodialysis equipment, caused an outbreak of nosocomial bloodstream infections. The active ingredient is the same chemical compound that is also registered under another name by the EPA as a chemical disinfectant and sterilizer. The FDA, like the EPA, does not perform laboratory tests in one of their own laboratories to assure the efficacy of such a disinfectant. I think this demonstrates clearly the difficulties a user has in recognizing the efficacy and the registered or approved uses of certain chemical disinfectants. Dr. Schaffner discussed this before.

In summary, ASM believes that the present lack of a declared governmental policy to monitor the efficacy and label claims of chemical disinfectants and sterilizers is a potential threat to the Nation's health through inadequate products which may not meet label claims. Even with the existence of a governmental testing facility, accidents happened in hospitals and led to unnecessary illness among our patients. The private sector, especially the hospitals of this country—trying very hard to reduce the Nation's medical expenses in accordance with Federal legislation—are unable to take over the Government's responsibility.

I hope that my presentation answered the questions posed in your letter of invitation.

In closing, I would like to ask you two questions:

One, who should be responsible for the testing and registration of chemical disinfectants and sterilizers for use in the health-care field? We have difficulty understanding the rationale that the use of a chemical germicide with a medical device has test approval requirements different from those of the EPA. Only one Federal agency should register and approve disinfectants.

Two, who is responsible to the public to assure the efficacy and label claims of chemical disinfectants and sterilizers? We believe that Congress has clearly stated, in FIFRA, that the Federal Government is responsible and not the user.

My colleagues and I thank you for the opportunity to express our opinion and I will be glad to answer some questions later.

[The prepared statement of Dr. Gröschel, together with attachments, follows:]

PREPARED STATEMENT OF DIETER H.M. GROSCHEL, M.D.

TESTIMONY

OF THE

AMERICAN SOCIETY FOR MICROBIOLOGY

Presented by

DIETER H.M. GRÖSCHEL, M.D., UNIVERSITY OF VIRGINIA
SCHOOL OF MEDICINE, CHARLOTTESVILLE

before the

SUBCOMMITTEE ON INVESTMENT, JOBS AND PRICES
of the
JOINT ECONOMIC COMMITTEE

Hearing on

"FEDERAL STANDARDS FOR AND FEDERAL TESTING OF HOSPITAL DISINFECTANTS"

August 7, 1986

Mr. Chairman and members of the Subcommittee, my name is Dieter Gröschel and I am Chairman of the Committee on Laboratory Practices for Microbiology of the Public and Scientific Affairs Board (PSAB) of the American Society for Microbiology (ASM). The ASM is pleased to have this opportunity to comment on the registration of chemical disinfectants and sterilizers for use in health-care institutions.

The ASM is the largest, single biological life science organization in the world with an active membership of over 34,000. The majority of its members are engaged in health-related work. Many are clinical microbiologists, infectious disease specialists, or hospital epidemiologists, and other scientists employed by educational institutions, pharmaceutical firms, and private and public laboratories where they work with microorganisms of medical importance. The success of microbiological research and of our professional services depends in part on the efficacy of chemical disinfectants and sterilizers. Members of the ASM have been involved in the formulation, evaluation and use of disinfectants as long as the Society has existed, since 1899.

In February 1983 we learned that the Office of Pesticide Programs of the Environmental Protection Agency (EPA) had ceased operation of its testing laboratory for disinfectant efficacy without public knowledge. I was concerned by the sudden change in policy and informed my colleagues in the field by writing an editorial which was published in the May/June 1983 issue of the journal, Infection Control, from which I quote:

> "Since 1946 the federal government, first under the Department of Agriculture and now under the EPA, has tested the efficacy of disinfectants available on the commerical market. The EPA has discontinued efficacy testing of disinfectants after registration

with the Agency. Chemical sterilizers which were pretested by EPA before granting registration are no longer subject to testing. This policy has been in effect since the summer of 1982. EPA registration of disinfectants, sporicides, virucides, fungicides, and sterilizers is now based solely on efficacy data submitted by the manufacturer. There is no federal government enforcement testing of commercially available products after registration is granted. The EPA believes such testing is redundant and that personnel who did the testing should be reassigned to higher priority needs.

"Congress has given the EPA, through the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), the means to assure the public that EPA registered disinfectants/sterilizers are effective when used as directed on the label. Now this is being ignored, apparently for budgetary reasons. For years we were advised, and reminded ourselves, that efficacy testing by the laboratories of the EPA gave assurance that the directions for use and claims of effectiveness of an EPA-registered germicide were valid. It appears that the government has silently abandoned its responsibility for the sake of cost reduction, while professing continued interest in protecting the public's health. Since we, the users of disinfectants and sterilizers, rely on the effectiveness of commercial products in many areas of our medical institutions - operating rooms, intensive care units, nurseries, isolation rooms - we are forced to find other means to guarantee the efficacy of disinfectants."

The ASM expressed its concerns to Mr. William Ruckelshaus, then EPA Administrator, in a letter of July 22, 1983, and requested information about the termination of the in-house testing program without public notice or explanation and about proposed alternatives to this program. The letter also stressed the importance of the EPA registration and label review for safeguarding public health. In the response by the Acting Assistant Administrator for Pesticides and Toxic Substances several reasons were given for closing the laboratories; two were of special interest to ASM: 1) the statement that the laboratory, in previous years, had screened preregistration samples and samples from the marketplace for postregistration enforcement only infrequently, and 2) that the Association of Official Analytical Chemists (AOAC) laboratory methods used to assess efficacy had to undergo revisions. The EPA letter stated that by "having removed the 'security blanket' of federal disinfectant testing... private sector groups...would have an interest in undertaking a credible testing program, but to date [August 18, 1983] little interest has been demonstrated. Though cognizant of the problem, individual hospitals do not appear to have adequate resources or the inclination to become involved." We agree with the EPA that hospital laboratories do not have the expertise and resources, due in part to the fiscal constraints imposed by the Tax Equity and Fiscal Responsibilities Act (TEFRA) and later Diagnostic-Related Group (DRG) legislation, to assume local testing. Nor do the forty-seven states without disinfectant testing programs, under the present budgetary constraints, have the resources or the capability to establish their own preregistration and enforcement testing programs according to FIFRA. It appeared to ASM that EPA was simply trying to find a reason to remove the testing laboratory activities from its budget and, therefore, ASM requested on October 20, 1983, a more detailed and scientific answer to its request for information. Copies of this correspondence were provided to several members of Congress including Senators Sarbanes and Stafford. In response, Mr. Ruckelshaus invited ASM to meet with the new Assistant Administrator for the Office of Pesticides and Toxic Substances, Dr.

John Moore. This meeting between representatives of ASM and Dr. Moore and two EPA associates took place on January 27, 1984. Dr. Edwin L. Johnson, Director of Pesticide Programs of the EPA, confirmed the termination of the disinfectant efficacy testing and presented the interest of EPA in two areas: 1) to improve existing methodology for official testing, and 2) to design a scheme for testing, monitoring and enforcement that is economic as well as effective. After some discussion Dr. Moore asked if ASM would be willing to explore with EPA the design of a program of efficacy and enforcement testing, possibly by contracting. The ASM agreed in principle to participate but only as one of several scientific organizations. It stressed that actions would be required on several levels which would include manufacturers, local and state agencies. This agreement was also stated in the summary letter by Dr. Moore to ASM.

Since then ASM has considered with other organizations a national symposium sponsored by ASM and supported by governmental, industrial and scientific organizations to discuss in detail the present status and future needs for testing and registering chemical disinfectants and sterilizers for use in the health care field. Planning is underway for a symposium in Washington, D.C., within the coming year.

Meanwhile, members of ASM have worked with EPA in reviewing existing and proposed testing procedures. The reason the ASM is concerned about the closure of the EPA Office of Pesticide's testing laboratory in 1982 is its worry about the way the federal government plans to assure the public that EPA-registered germicides (chemical disinfectants and sterilizers) are safe and effective as claimed on the labels of such preparations. The discussion among microbiologists, nurses, hospital epidemiologists and other health-care professionals has addressed the responsibility of the federal government to the public and the reasons for removing the federal "security blanket" in the field of disinfection and sterilization. As consultants to our institutions we are responsible for disinfection and sterilization in hospitals, operating rooms, nurseries, intensive care units, clinics, and other health-care institutions. The EPA's action has placed us and our patients at risk. We cannot understand how a federal agency charged by the law to ensure efficacy and to enforce regulation can abrogate its responsibility making the user finally responsible. I would like to give you two examples from the recent literature as justification of our concerns. Both instances occurred even before the closure of the EPA laboratories. One is the famous Serratia marcescens outbreak in Florida complicating cardiopulmonary operations. It was traced to a disinfectant contaminated with this organism and was reported by Ehrenkranz et al, in Lancet II, on December 13, 1980 (p. 1289). The other report concerned the failure of a chemical disinfectant to prevent the transmission of Salmonella newport through a sigmoidoscope that had been used on a patient infected during a food-borne outbreak in the Midwest (Holmberg et al. New England Journal of Medicine, 311:617, 1984). Both disinfectants were EPA-registered for use with related bacteria. As with all nosocomial infections the patient pays the bill.

We believe that the federal government should show leadership in reviewing and updating the existing official test methods for chemical disinfectants and sterilizers which many experts consider antiquated. A few years ago, tests in a manufacturer's laboratory showed that the presently required AOAC test for tuberculocidal activity cannot be applied to all chemicals and all use situations; the manufacturer proposed a new quantitative test methodology. The EPA responded to this finding by calling two Scientific Advisory Panel subpanel meetings. As a result of these meetings and public comments, also due to the urging of certain interest groups, EPA recently published a policy on testing methods (Federal Register 51, No. 102, 19-70, 1986) stating that the new quantitative test methodology for tuberculocides is acceptable but that the old AOAC method is still accepted for registration if either modified as to time and/or temperature of testing, or, in the case of glutaraldhydebased and quaternary ammonium compounds, is supported by validation data from a second testing facility. Many professionals in the field believe that this second testing facility should be a governmental laboratory, preferably at the EPA.

We are also concerned that there are two different federal agencies involved in regulation and testing of chemical germicides, FDA and EPA. The FDA is charged by law to approve antiseptics and EPA registers chemical disinfectants and sterilizers. However, if a disinfectant is used to decontaminate a medical device, the test results submitted by a manufacturer are reviewed and approved by FDA as accessory to a device. Recently, the bacterial contamination of a device-disinfecting agent approved by FDA for decontaminating hemodialysis equipment caused an outbreak of nosocomial blood stream infections (Morbidity and Mortality Weekly Report 35:417, 1986). The active ingredient of the disinfectant is the same chemical compound that is registered under another name by EPA as a chemical disinfectant and sterilizer. The FDA, like the EPA, does not perform laboratory tests in one of their own laboratories to assure the efficacy of a disinfectant. This demonstrates the difficulties a user has in recognizing the efficacy and registered or approved use of certain chemical disinfectants.

In summary, ASM believes that the present lack of a declared governmental policy to monitor the efficacy and label claims of chemical disinfectants and sterilizers is a potential threat to the nation's health through inadequate products which may not meet label claims. Even with the existence of a governmental testing facility accidents happened in hospitals and led to unnecessary illness among patients. The private sector, especially the hospitals of this country - trying very hard to reduce the nation's medical expenses in accordance with federal legislation - are unable to take over the government's responsibility. I hope that my presentation answered the questions posed in your letter of invitation.

In closing, I would like to ask two questions:

1) Who should be responsible for the testing and registration of chemical disinfectants and sterilizers for use in the health-care field? We have difficulty understanding the rationale that the use of a chemical germicide with a medical device has test and registration/approval requirements different from those of the EPA. Only one federal agency should have the responsibility to register or approve.

2) Who is responsible to the public to assure the efficacy and label claims of chemical disinfectants and sterilizers? We believe that the Congress has clearly stated in FIFRA that the federal government is responsible and not the user.

My colleagues and I thank you for the opportunity to express our opinion and I will be glad to answer any questions.

Brief Biographical Sketch of Dieter H. M. Gröschel, M.D.

Graduate Physician (equivalent to M.D. in USA), University of Cologne, Germany, 1957.
Doctor medicinae, University of Cologne, Germany, 1958.
Diplomate, American Board of Medical Microbiology, 1965.

Professor of Pathology and Internal Medicine, Director of Microbiology, University of Virginia School of Medicine, Charlottesville, Virginia, 1979 to present.

Associate Professor and Professor of Pathology, Chief, Section of Microbiology, and Infection Control Officer, University of Texas System Cancer Center M.D. Anderson Hospital and Tumor Institute, Houston, Texas, 1971-1979.

Director of Microbiology and Infectious Diseases and Infection Control Officer, Springfield Hospital Medical Center, Springfield, Massachusetts, 1968-1971.

Assistant and Associate Professor of Microbiology, Temple University School of Medicine, Philadelphia, Pennsylvania, 1965-1968.

Associate, Wistar Institute, Philadelphia, Pennsylvania, 1963-1965.

Member and Chairman of institutional Infection Control Committees, 1965 to present.

Member of institutional Biosafety Committees, 1974 to present.

Editor, Handbook on Hospital-Associated Infections, Vol. 1-3, Dekker, New York, 1978-1979; Handbook of Antisepsis, Verlag Volk and Gesundheit, Berlin, 1981 to present; Laboratory Safety: Principles and Practice, Am. Soc. Microbiol., Washington, 1986.

Joan Knock of the University of Reading who handled all the data, prepared the computer programmes, and analysed the data.

Requests for reprints should be addressed to W. E., West Berkshire Health District, 3 Craven Road, Reading, Berks RG1 5LF.

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Hospital Practice

ANTIBIOTIC-SENSITIVE *SERRATIA MARCESCENS* INFECTIONS COMPLICATING CARDIOPULMONARY OPERATIONS: CONTAMINATED DISINFECTANT AS A RESERVOIR

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Summary A cluster of *Serratia marcescens* infections complicating cardiopulmonary bypass operations was traced to contaminated quaternary ammonium disinfectant. Failure of hospital personnel to clean the disinfectant spray bottles before refilling them had enabled the organisms to survive and contaminate the environment, including the extracorporeal circulator. The organisms grew in two of four formulations of quaternary ammonium disinfectant. *Serratia* sensitivity to ampicillin and tetracycline was an epidemiological marker of a common-source outbreak.

INTRODUCTION

Serratia marcescens has a wide distribution in nature and thrives in moisture. It is not generally part of healthy human microbial flora,[1] although the organism has been recovered from hands of hospital personnel,[2-6] which have become transiently colonised after contact with infected patients' secretions or contaminated solutions. Quaternary ammonium disinfectants are widely used in hospitals to reduce the number of such microorganisms in the environment and prevent cross-infection. Unfortunately, contamination with some *Pseudomonas aeruginosa* or *Ps. cepacia* strains which are inherently capable of growth in the disinfectant can lead to outbreaks of infection.[7,8] This report describes a cluster of nosocomial infections due to *S. marcescens* distributed in a quaternary ammonium disinfectant. The infecting strain was unique in its ability to multiply in some but not all quaternary ammonium disinfectants and had a distinct marker of antibiotic sensitivity.

CASE CLUSTER AND DEMONSTRATION OF CIRCULATOR CONTAMINATION

In June and July, 1978, two patients at one hospital developed transient *Serratia* bacteraemia after cardiac operation requiring cardiopulmonary bypass with extracorporeal circulation. In August, 1978, the infection-control nurse initiated surveillance cultures of the extracorporeal circulator during each of eleven operations. Immediately before connection of the patient for cardiopulmonary bypass the Ringer's lactate solution used for priming the circulator was withdrawn for culture, and during the operation the patient's blood in the circulator was similarly cultured. Circulator contamination with *Serratia* was demonstrated in nine operations—two for aortic-valve replacement, three for mitral-valve replacement, and four for coronary-artery bypass. In three instances, circulator cultures made both before and after connection of the patient yielded *Serratia*. Two of these patients subsequently developed *S. marcescens* sternal-wound infection. In six operations, only the culture made during patient use yielded *Serratia*. One of these patients later developed endocarditis and required replacement of an aortic valve for cure; *S. marcescens* was cultured from the infected valve. Another patient eventually manifested *S. marcescens* sternal-wound infection.

INVESTIGATION

Review of operating-room practices and procedures for these operations revealed no apparent departures from standard practice, except on occasion when the circulator pressure manometer was not removed and sterilised after use, although this generally was done. Preoperative and postoperative antibiotic prophylaxis included cephalothin and gentamicin treatment. After each operation all circulator tubing was discarded. Fresh sterile tubing was connected immediately prior to operation.

More than 300 surveillance cultures of equipment, medications, disinfectants, room and equipment surfaces, air, fluids, and hands of operating-room personnel were made. Hands of one of two circulator technicians, the sink drain in a utility room, the ice chest used for intraoperative storage of chilled intravenous fluids, and three of four bottles of A33 disinfectant solutions in a spray bottle yielded *S. marcescens*. Intravenous fluids and ice sampled before storage in the ice chest, fluids used for the circulator, and the dry disinfectant yielded no *Serratia*.

A33 disinfectant had been in hospital use for six years and was sprayed preoperatively in the cardiac operating room as an environmental disinfectant. It was applied to the floor adjacent to the extracorporeal circulator, an area the pump technician touched while connecting tubes for priming the circulator. The dry disinfectant was freshly prepared and diluted in tap-water according to manufacturer's directions. However, spray bottles were refilled when partially empty and were not regularly emptied and cleaned before refilling.

After recognition of contamination in September, A33 was withdrawn from use and environmental disinfection of the operating room with spray bottles was discontinued. Cultures from the hands of technicians and other personnel no longer yielded *Serratia*. The pressure manometer was now routinely disassembled and sterilised. Surveillance cultures from the extracorporeal circulator before and during connection of the patient in seven operations were now sterile. No further episode of *Serratia* bacteraemia was detected in a 24-month follow-up.

METHODS

Surveillance Cultures

Cultures were made from the hands of physicians and operating-room personnel at the end of an operation after removal of sterile gloves, by immersion and rinsing of the hands in 10 ml of nutrient broth in a sterile plastic bag. Hands of ungloved personnel were similarly cultured during an operation. Airborne bacteria in the operating room were sought by exposure of blood-agar plates during operation. Swabs of floor and other surfaces, air-conditioning filters, and ice were placed into thioglycolate broth for culture. Fluids were cultured by aseptic transfer of 5 ml into 50 ml broth.

Identification of Organisms

Isolates were identified with standard biochemical procedures.[9] Antimicrobial susceptibility tests were done by the disc-diffusion method based on the Bauer-Kirby procedure[10,11] and the broth-dilution method[12] using 'Sensititre' plates (Gibco Diagnostics). The isolates were serotyped at the Center for Disease Control, Atlanta, Georgia.

Disinfectants

Four quaternary ammonium disinfectants were tested. A33 Dry (Airkem Laboratories) contained n-alkyl (60% C14, 30% C16, 5% C18, 5% C12) dimethylbenzyl ammonium chloride (5·8%) and n-alkyl (68% C12, 32% C14) dimethyl ethylbenzyl ammonium chloride (5·7%), the in-use dilution being 1:256; TBQ (Vestal Laboratories) contained N, N, bis 2-omegahydroxypoly (oxyethylene) ethyl alkylamine (12%) and n-alkyl (50% C14, 40% C12, 10% C16) dimethyl benzyl ammonium chloride (8%), the in-use dilution being 1:256; TOR (Huntington Laboratories) contained n-alkyl (60% C14, 30% C16, 5% C18, 5% C12) dimethyl benzyl ammonium chloride (1·6%) and n-alkyl (50% C12, 30% C14, 17% C16, 3% C18) dimethyl ethylbenzyl ammonium chloride (1·6%), the in-use dilution being 1:64; and HI-TOR (Huntington Laboratories) contained n-alkyl (60% C14, 30% C16, 55% C18, 5% C12) dimethyl benzyl ammonium chloride (6·75%) and n-alkyl (68% C12, 32% C14) dimethyl ethylbenzyl ammonium chloride (6·75%), the in-use dilution being 1:128. Solutions were prepared according to the manufacturer's instructions.

Microbial Susceptibility to Disinfectants

Organisms for testing were prepared from isolated colonies on a 5% sheep-blood agar plate which was incubated overnight. Bacterial cells were washed twice with deionised water, and the suspension was diluted to the desired concentration; 0·05–0·1 ml was used as an inoculum for 5–10 ml of disinfectant. The mixture was maintained at room temperature and samples were taken periodically to determine microbial viability. A disinfectant-resistant population of cells was maintained by continuous exposure to A33 disinfectant. The number of viable cells which could be maintained in the disinfectant was approximately 10^7 organisms/ml.

Conjugation

R-plasmid transfer experiments were attempted with a disinfectant-resistant isolate and a disinfectant-sensitive isolate using a modification of the procedure of Suenderhaul et al.[13]

Sudan-black B Stain for Bacterial Fat

Increased intracellular fat, considered an indicator of lack of permeability to quaternary ammonium disinfectant,[14] was determined with the Sudan-black B stain method as described by Chaplin.[14] Cells maintained in the A33 disinfectant for 7 days were harvested by filtration using 0·25 μm pore size filters (Millipore Corporation) and resuspended in deionised water before staining. Cells containing fat are darkly stained.

Calcium Determinations

Calcium-ion concentration in the water used to prepare the disinfectants was determined by atomic absorption spectrophotometry.[15]

RESULTS

Eight *S. marcescens* isolates from infected patients and surveillance cultures were serotyped. In one a somatic antigen was identified. Others could not be serotyped with the available 01–020 anisera. Isolates from one disinfectant bottle, the ice chest, and two patients were motile. The motile isolates possessed flagella antigen H8. Antibiotic-susceptibility testing showed that isolates were resistant only to cephalothin (see table).

Eight *S. marcescens* isolates obtained during the outbreak repeatedly survived exposure to A33 but were regularly killed by TOR and TBQ. On occasion isolates survived exposure to HI-TOR. *S. marcescens*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, and *Ps. cepacia* strains recovered from patients in other hospitals were killed by all disinfectants tested.

A minimum inoculum of 10^7 organisms/ml was necessary for the *Serratia* isolate to survive in A33 disinfectant. When A33 disinfectant solution was inoculated to a density of approximately 6×10^8 organisms/ml using organisms from an overnight growth on 5% sheep-blood agar, the viable count dropped to 10^1/ml within an hour of exposure at room temperature (fig. 1); however, continued incubation resulted in microbial multiplication. After 4 days the colony count

SEROTYPE AND ANTIBIOTIC SUSCEPTIBILITY OF *SERRATIA MARCESCENS* ISOLATES FROM THE CASE CLUSTER

Source	Serotype*	Minimal inhibitory concentration (μg/ml)							
		AMP	CB	CF	AMK	GM	K	CH	TET
Blood—Patient A	0 undetermined: H8	1	<4	32	0·5	0·5	2	2	2
Wound—Patient B	0 1 : NM	2	<4	64	2	0·5	2	8	4
Circulator—Patient C	0 rough : H8	2	<4	64	1	0·5	2	8	4
Circulator—Patient D	0 undetermined: NM	2	<4	128	2	1	2	8	4
Technician—hands	0 undetermined: ISM	2	<4	64	2	0·5	2	4	4
Disinfectant	0 undetermined: H8	2	<4	128	2	1	2	4	4
Disinfectant	0 undetermined: NM	4	<4	128	4	1	4	8	8
Ice chest	0 undetermined: H8	2	<4	128	2	2	4	4	4

AMP = ampicillin; CB = carbenicillin; CF = cephalothin; AMK = amikacin; GM = gentamicin; K = kanamycin; CH = chloramphenicol; TET = tetracycline.
*0 refers to the somatic antigen; H the flagella antigen; NM = non-motile; ISM = insufficiently motile for testing.

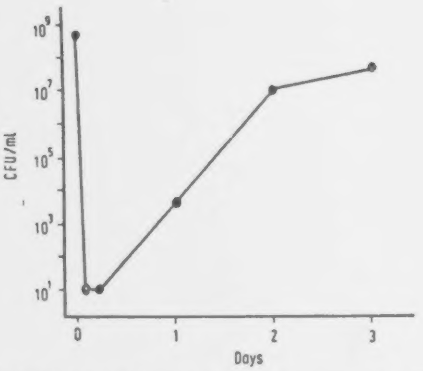

Fig. 1—Survival and growth of *Serratia marcescens* in A33 disinfectant at room temperature.

reached a plateau of 10^7/ml. The isolate when inoculated into tap-water, deionised water, or triple-distilled water at a concentration of 10^2/ml, grew to 10^5–10^6/ml within 4 days of incubation at room temperature.

Cells which grew in the disinfectant were harvested by centrifugation and re-exposed to fresh disinfectant at concentrations of 10^1 and 10^6/ml. These populations of cells had not decreased at 1 h but continued to multiply.

A33-disinfectant-resistant cells were tested against other quaternary ammonium solutions prepared in tap-water. Growth of A33-resistant cells occurred in A33 and HI-TOR disinfectants but not in TBQ or TOR disinfectants (fig. 2).

Tap-water contained 2·3 mg calcium/dl. Adding ethylenediamine-tetra-acetate (EDTA) to tap-water did not alter the susceptibility of the A33-resistant cells. A33 prepared with deionised water and inoculated with A33-disinfectant-resistant cells resulted in complete kill.

Conjugation experiments to test whether resistance was plasmid-mediated revealed no transconjugates.

A33-disinfectant resistant and susceptible cells examined with Sudan-black B stain for cell fat revealed no difference in staining intensity.

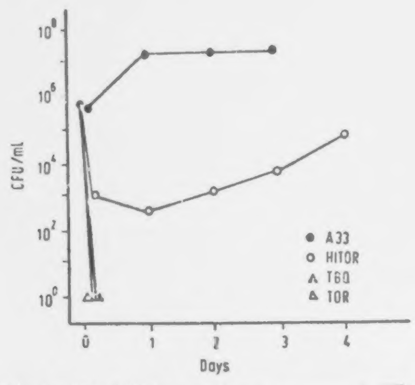

Fig. 2—Survival of A33-resistant *Serratia marcescens* in different quaternary ammonium disinfectants.

DISCUSSION

Persistence and growth of *Serratia* in the A33 disinfectant resulted from refilling of partially empty spray bottles. The contaminated disinfectant was sprayed on various operating-room surfaces, including the circulator, immediately before operation. The circulator is likely to have been contaminated from the technician's hands when he connected tubes for priming. On those occasions when the pressure monitor was not changed, it could have served as a secondary source of contamination. The danger of using quaternary ammonium compounds as disinfectants rather than cleansers is re-emphasised.[16] Hospital personnel cannot be relied upon to distinguish between disinfectants which can and cannot support microbial growth, although they should be expected not to top up solutions.

Serotyping of the *S. marcescens* isolates showed that only one isolate had an identifiable somatic antigen and several motile isolates had a common flagellar antigen. The somatic antigen in most of the isolates could not be determined. This suggests at least two populations of resistant cells. Interspecies transfer of genetic material carrying a resistance marker was not demonstrated.

The similarity in composition of the dimethyl benzyl ammonium and dimethyl ethylbenzyl ammonium chains in A33 and HI-TOR disinfectants which supported *Serratia* growth is noteworthy. In contrast, neither TOR, which possessed a more complex dimethyl ethyl benzyl ammonium chain, nor TBQ, a dimethyl benzyl ammonium disinfectant that also contained an ethyl alkylamine compound, permitted growth. Tap-water but not distilled water diminished A33 disinfectant activity against the outbreak strain of *Serratia*. Quaternary ammonium compounds alter bacterial-cell membranes, and their activity is generally enhanced by EDTA.[17] Resistant strains of *Serratia* are reported to have extra lipid. However, the resistant isolates in this outbreak were not rendered sensitive in tap-water by EDTA, nor was increased fat demonstrated.

Many *Serratia* found in soil and water outside the hospital are sensitive to antibiotics (other than penicillin G, cephalothin, and colistin), whereas those recovered in hospitals are generally resistant to ampicillin and tetracycline.[18,19] *Serratia* outbreaks attributed to cross-infection of patients are characterised by plasmid-mediated antibiotic-resistance patterns and are associated with considerable antibiotic usage.[1] In this common-source outbreak the isolates were susceptible to ampicillin and tetracycline. In five of ten common-source outbreaks mentioned by Farmer and others, similar antibiotic-sensitive *Serratia* were described.[19]

We thank the Airwick and Vestal Companies for supplies of disinfectant reagents and Vestal for financial support. We also thank Dr D. Brenner and Ms B. Davis, of the Center for Disease Control, for aid in serotyping of *Serratia*.

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Infant Feeding

DOES A CHANGE IN THE COMPOSITION OF HUMAN MILK AFFECT SUCKING PATTERNS AND MILK INTAKE?

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Summary Human breast milk of high and low fat content was fed to twenty-four babies aged 4–9 days from bottles. Changes in fat content parallel to those found during the course of a breast-feed (i.e., switching the baby from low-fat breast milk to high-fat breast milk) did not alter either milk intake rate or sucking patterns.

INTRODUCTION

WHEN a baby is nursed at the breast the composition and flow of milk change over time; the fat content increases and the flow rate decreases.[1,2] Hall[3] proposed the hypothesis that changes in the composition of milk towards the end of a feed on each breast might be a cue for the baby to stop feeding; if so, this change could be important in the regulation of milk intake. This appealing idea has been widely quoted.[4-9]. But it has yet to be subjected to any experimental test.[10] We report such a test. Human breast milk of high and low fat content was fed to babies from bottles, and sucking patterns and milk intake rates were recorded.

MATERIALS AND METHODS

Milk

Breast milk was obtained in the John Radcliffe Hospital from mothers with babies under 10 days of age. They collected surfeit milk in Waller shells which were worn between feeds, and from the unsuckled breast during feeds.[11]

Of an initial 200 ml of milk, about 160 ml was centrifuged for 15 min at 1500 rpm and 4°C. The fat layer was removed and added to the remaining 40 ml. This procedure yields one part of high-fat milk to four parts of low-fat milk. The high-fat and low-fat milk were then each remixed and pasteurised by the holder method (heating to 63°C for 30 min, then cooling rapidly to below 18°C for 40 min before refrigeration).[11] A sample of milk from each batch was used for bacteriological culture. The batch was accepted if there was no growth of potentially pathogenic organisms—i.e., <5/ml of any organism other than *Staphylococcus albus*, *S. epidermis*, and airborne or aerobic spore-bearing bacilli. The milk was used at once, or stored at −20°C after pasteurisation if there was no suitable baby requiring an immediate feed. The milk was transferred to sterile feeding bottles immediately before use, and fed at room temperature.

The method produced an average 4·1-fold difference in fat content, as determined by the creamotocrit method.[12] This is at least as high as the average difference between foremilk and hindmilk found by Hytten,[1] and the largest difference for an individual in his work and milk used in this study is comparable (0·45–10·15 g/dl and 0·56–10·40 g/dl, respectively).

Equipment

'Freeflo' bottles (Lewis Woolf Griptight), with one teat aperture (size 0·4–0·5 mm), were fitted with a manometer tube (length 60 cm, internal diameter 1·5 mm), terminating at the apex of the teat. The tube was connected to a Statham pressure transducer and sucks were recorded automatically onto magnetic tape. Criterion for a suck was any reduction in intra-oral pressure falling below a threshold of −75 mmHg. The magnetic tapes were analysed by computer to give a serial record of all intersuck intervals. The bottles were sterilised in hypochlorite solution ('Milton') before each feed.

Subjects

Twenty-four bottle-fed babies were tested at 4–9 days of age. There were twelve boys and twelve girls; mean birthweight was 3287 g (SE±89 g). We studied bottle-fed babies because we did not want to risk any disruption of the early stages of breast-feeding.

Procedure

Two bottles, each containing about 40 ml of the milk were mixed for each feed. These quantities were designed to be in excess of average intake at this age (about 70 ml). The baby was fed for a maximum of 5 min on each bottle, and winded between bottles as necessary. Eight babies (experimental group) were fed low-fat followed by high-fat milk. This simulates the change during breast-feeding. Eight were fed low-fat followed by low-fat milk (control group I). A further eight were fed high-fat followed by low-fat milk (control group II); this controls for change as such, rather than change from low-fat to high-fat milk. All babies were fed the test milk by a research sister (P. J. Lucas).

RESULTS

Milk Intake Rate

Fig. 1 shows the rate of milk intake on low-fat and high-fat milk. Two separate statistical analyses were carried out, with *t* tests for unrelated samples. Firstly we calculated for each baby the difference in intake on the first and second bottle,

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DR EHRENKRANZ AND OTHERS REFERENCES—*continued*

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DRUG-RESISTANT SALMONELLA FROM ANIMALS FED ANTIMICROBIALS

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Abstract It has been difficult to document the postulated sequence of events that begins with the selection of drug-resistant organisms in animals fed subtherapeutic amounts of antimicrobials and ends with clinically important infections in human beings. In early 1983 we identified 18 persons in four Midwestern states who were infected with *Salmonella newport* that was resistant to ampicillin, carbenicillin, and tetracycline and characterized by a 38-kilobase R plasmid. Twelve of these patients had been taking penicillin derivatives for medical problems other than diarrhea in the 24 to 48 hours before the onset of salmonellosis. Eleven patients were hospitalized for salmonellosis for an average of eight days, and one had a fatal nosocomial infection. We compared plasmid profiles of all human (six-state area) and animal (United States) *S. newport* isolates over an 18-month period and examined selected records of meat distribution. The results indicated that the patients had been infected before they took antimicrobials, by eating hamburger originating from South Dakota beef cattle fed subtherapeutic chlortetracycline for growth promotion.

This study demonstrates that antimicrobial-resistant organisms of animal origin cause serious human illness, and emphasizes the need for more prudent use of antimicrobials in both human beings and animals. (N Engl J Med 1984; 311:617-22.)

VARIOUS gastrointestinal illnesses — from mild, self-limited diarrhea to pseudomembranous colitis — are recognized complications of treatment with antimicrobials.[1] Less appreciated, however, is the clinical expression of previously asymptomatic infections with antimicrobial-resistant enteric bacteria after the use of antimicrobials. Only a single case of severe illness due to antimicrobial-resistant salmonella beginning after antimicrobial therapy has been previously reported.[2]

Multiple drug-resistant isolates have accounted for a steadily increasing percentage of human salmonella infections[3] and now represent approximately 20 to 25 per cent of identified cases.[4,5] The source of these resistant enteric pathogens in persons is controversial,[6-8] but many believe that subtherapeutic amounts of antimicrobials administered to animals in their feed for "growth promotion" or "disease prevention" select for resistant bacteria that eventually infect people. About half the antimicrobials produced in the United States yearly are fed to farm animals, but proof of the emergence of drug-resistant enteric pathogens in food animals fed subtherapeutic amounts has been difficult to obtain because of the complex sequence of events between farming practices and human disease.[9]

In early February 1983, laboratory-based surveillance of salmonella infections by the Minnesota Department of Health showed that there was a marked increase in isolates of *Salmonella newport (S. enteritidis* serotype *newport)* and that many of the patients contacted had been taking antibiotics for nondiarrheal illnesses just before the onset of salmonellosis. An investigation was begun to examine the possibility that the outbreak was caused by a contaminated antimicrobial. This hypothesis was rejected since the patients had taken different antimicrobials from different pharmacies and manufacturers. We describe here the results of subsequent investigations in a six-state area, which indicated that taking antimicrobials may provide a selective advantage for resistant enteric bacteria causing serious illness, and that food animals were the source of the multiply resistant *S. newport*.

METHODS

All patients in a recognized cluster of 10 cases of *S. newport* infection in Minnesota (early 1983) were interviewed for histories of foods eaten, antimicrobial use, clinical illness, hospitalization, travel, and illness in family members. For comparison with the outbreak cases, we interviewed and obtained isolates from 11 of 12 patients with *S. newport* infections that were reported to the Minnesota Department of Health in 1982 and from 27 of 30 patients with salmonellosis (serotypes other than *S. newport*) reported in Minnesota in the first two months of 1983.

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Table 1. Findings in 18 Cases of Multiply Resistant *S. newport* Infection.

Patient No	Age/Sex	Date of Onset	Antimicrobial (Date Started)	Days in Hospital	Hamburger from Herd *	Comments
South Dakota outbreak						
1	29/F	12/13/82	Amoxicillin (12/11)	17	Yes	
2	3/F	12/13/82	Amoxicillin (12/11)	4	Yes	Daughter of Pt 1
3	69/M	12/27/82	Multiple (12/15–1/10)	13 †	No	Secondary case ‡
4	33/M	2/14/83	Penicillin (2/11)	8	Yes	Dairy-herd owner
Minnesota outbreak						
5	20/M	1/18/83	Penicillin (1/10)	5	Yes	
6	33/F	1/26/83	Amoxicillin (1/25)	8	Yes	
7	43/F	1/28/83	None	0	Yes	
8	43/F	1/29/83	None	0	No	
9	20/F	1/31/83	None	6	Yes	"Cold" (1/24)
10	34/F	2/1/83	Penicillin (1/26)	0	No	
11	8/F	2/1/83	Amoxicillin (1/30)	4	No	
12	33/M	2/2/83	Amoxicillin (1/31)	5	Yes	Husband of Pt 6
13	20/F	2/6/83	Amoxicillin (2/4)	13	Yes	
14	37/F	2/8/83	Penicillin (2/7)	0	Yes	
Other cases						
15	18/F	2/5/83	None	0	No	North Dakota
16	30/M	2/10/83	Penicillin (2/8)	6	Yes	Iowa
17	6/M	4/14/83	None	0	Yes	Son of Pt. 4
18	17/M	5/4/83	None	0	Yes	Son of Pt. 7

*Hamburger at home supplied directly from the suspected herd or purchased from markets thought to be supplied with meat from the herd.

†Days between onset of diarrhea and death in hospital.

‡Patient underwent endoscopy directly after Patient 1.

After the investigation in Minnesota, we reviewed state and federal surveillance records for Minnesota, South Dakota, North Dakota, Iowa, Wisconsin, and Nebraska and obtained all available human isolates of *S. newport* in the six-state area for 1982 and the first half of 1983. After determining which isolates had the same pattern of antimicrobial resistance and the same plasmid profile as the isolates from the outbreak in Minnesota, we interviewed the patients for the same information as obtained from the patients in the Minnesota outbreak.

All salmonella isolates, including those from comparison groups, were tested for antimicrobial resistance by means of standard Kirby–Bauer disks.[10] The plasmid DNA from *S. newport* isolates resistant to ampicillin, carbenicillin, and tetracycline was analyzed according to a modification of a technique described by Birnboim and Doly.[11] Plasmids were further characterized by restriction-endonuclease digestion with *Hind*III according to the manufacturer's instructions (Bethesda Research Laboratories).

To determine whether antibiotic resistance was plasmid-mediated (R plasmid), we attempted to transfer resistance from the epidemic *S. newport* by broth and filter matings with nalidixic acid–resistant strains of *Escherichia coli* (185 and C600) and rifampin-resistant *S. heidelberg*. In addition, *E. coli* C600 was transformed with plasmid DNA extracted from *S. newport* isolates from the outbreak and comparison groups.[12] We attempted to cure *S. newport* of antibiotic resistance by growth at 42°C and by exposure to varying concentrations of acridine orange, sodium dodecyl sulfate, and ethidium bromide.[11] Plasmid DNA was hybridized with a ^{32}P-labeled beta-lactamase gene probe (prepared by Robert C. Cooksey, Ph.D., Centers for Disease Control). The probe was obtained by electroelution of a 1-kb (kilobase) fragment after sequential restriction-endonuclease digestion of pBR322 plasmid DNA with *Eco*RI and *Hinf*I.

We obtained all available *S. newport* strains isolated from livestock and poultry in the six-state area in 1982 and the first half of 1983, as well as all nonhuman strains isolated in the United States from October 1981 through September 1982 (U.S. Department of Agriculture, National Veterinary Service Laboratory, Ames, Iowa). If livestock isolates showed the same antimicrobial-resistance pattern and plasmid profile as those from the outbreak group, we contacted owners about feeding, purchasing, sales, and antimicrobials added to feed for their herds. The distribution of all products from these herds was traced, when applicable, through sales, processing, and distribution centers.

RESULTS

In the initial investigation in Minnesota, we identified 10 patients with multiply resistant *S. newport* infection with dates of onset between January 18 and February 8, 1983. These patients ranged in age from 8 to 43 years (mean, 30; median, 33)(Table 1); eight lived in the Minneapolis–St. Paul metropolitan area (Fig. 1). Of the 10 cases, 7 had taken amoxicillin or penicillin in the week before the onset of illness (Table 1); 2 had taken leftover antibiotics without physician supervision. Five of the seven using antimicrobials had started taking penicillin derivatives within the 48 hours before the onset of symptoms of salmonellosis. Four users of amoxicillin had been taking it for bronchitis (two patients), thyroiditis (one patient), or otitis media (one patient); three users of oral penicillin took it for pharyngitis. The duration of illness before patients took antimicrobials was 1 and 3 days for the two patients with bronchitis and 2, 4, and 21 days for the three patients with pharyngitis, respectively. One person who had not taken antimicrobials before illness had had symptoms of a "cold" in the week before the onset of salmonellosis. In contrast, none of 11 patients with sensitive *S. newport* infections in 1982 had taken penicillin derivatives in the four weeks before their illnesses ($P = 0.001$, odds ratio = 51.3 [Fisher's two-tailed exact test]), and only 2 of 27 patients with recent non-*S. newport* salmonellosis had taken antimicrobials (cephaloridine or amoxicillin) in the four weeks before their illnesses ($P = 0.0004$, odds ratio = 29.2). None of 30 household contacts of the 10 patients in the Minnesota outbreak took antimicrobials or became ill, except for the contact who was also a patient (Patient 12).

Six of the Minnesota outbreak group were hospitalized for salmonellosis for an average of eight days (Table 1). All 10 in the group had diarrhea (defined as three or more loose stools in 24 hours), abdominal cramps, and nausea. Nine patients had documented fever (temperature above 38°C) with concurrent chills, eight had one or more episodes of vomiting, and six had blood in their stools.

In the subsequent investigation in the six-state area, we found four more cases of infection in South Dakota (Patients 1 through 4) with *S. newport* of the same antimicrobial-resistance pattern as in the Minnesota cases; all four patients had taken penicillins — one without physician supervision — before the onset of salmonellosis (Table 1). Patients 1 and 2 had had bronchitis for seven days before they took amoxicillin, and Patient 4 had had pharyngitis for four days before he took penicillin. Patient 3 (Table 1) had been admitted to the same hospital as Patient 1 for abdominal trauma, which was treated by splenectomy; diarrhea developed eight days after sigmoidoscopy, which had been performed in preparation for hemicolectomy. Hospital records showed that Patient 3 underwent sigmoidoscopy immediately after Patient 1, and that his endoscopy was performed by the same staff and with the same equipment. The sigmoidoscope had been put for 10 minutes in a glutaraldehyde-phenate solution (0.13 per cent glutaraldehyde) that had been in use for about 25 days. During his hospital stay, Patient 3 received many antimicrobials and died with fever, confusion, and other symptoms of septicemia 20 days after the endoscopy. *S. newport* resistant to ampicillin, carbenicillin, and tetracycline was isolated from blood, sputum, and stool before he died.

The isolates from the 10 cases in Minnesota and the isolate available from one case in South Dakota (Patient 4) were all resistant to ampicillin, carbenicillin, and tetracycline and had the same plasmid profile and endonuclease restriction pattern of plasmid DNA (Fig. 2). These characteristics were identical to those of an *S. newport* strain isolated from the tissues of a calf that died during an outbreak of diarrheal disease in Patient 4's dairy cows in November 1982 (Fig. 2).

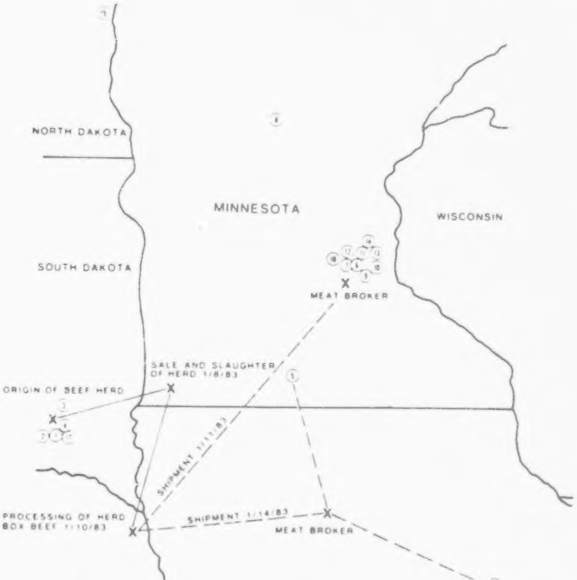

Figure 1. Distribution of 18 Cases of Resistant *Salmonella newport* Infection (Circled Numerals) in Relation to Origin and Shipment of Infected Beef, December 1982 through June 1983.

Broken lines denote suspected routes of shipment.

From laboratory analysis of 72 human isolates submitted to health-department laboratories in the six-state area from January 1982 through June 1983, we found four more *S. newport* isolates with the epidemic antimicrobial-resistance pattern and distinctive 38-kb plasmid seen in outbreak isolates. The four cases of the epidemic *S. newport* strain occurred during or after the 14 cases of the outbreaks in Minnesota and South Dakota. Two of the four patients (Patients 17 and 18) lived with outbreak patients (Patients 4 and 7); we were unable to determine whether their infections were acquired from food also eaten by outbreak patients (frozen hamburger or raw milk) or from secondary spread from outbreak patients. Patient 16 (Iowa) was ill during the outbreak in Minnesota. Like many of the outbreak patients, he had taken an antimicrobial before becoming ill (penicillin for a sore throat during the two days before the onset of diarrhea) and was hospitalized for salmonellosis (Table 1). Before her illness Patient 15 (North Dakota) ate most of her meals at a college cafeteria and was unable to specify the foods eaten. An additional isolate obtained from a patient in Wisconsin in 1982 contained the 38-kb plasmid, but in association with a 5.1-kb plasmid that was not present in the outbreak isolates; moreover, this patient acquired the infection in Mexico or Texas.

Epidemiologic investigation in Minnesota to determine the source of the epidemic *S. newport* revealed that the patients had eaten no unusual foods, but all had eaten ground beef (hamburger) in the week before illness. Seven of the 10 patients in Minnesota were women who prepared food, among whom two said they might have tasted raw hamburger before cooking it. Three South Dakota patients (No. 1, 2, and 4) lived on two farms and were related by marriage, but they had not eaten together or socialized with one another in the previous year. The only common place of exposure for these patients was a relative's feedlot beef farm, which was adjacent to the farm of Patient 4's dairy herd. Patients 1, 2, and 4 had received beef directly from the beef herd in 1982 and 1983.

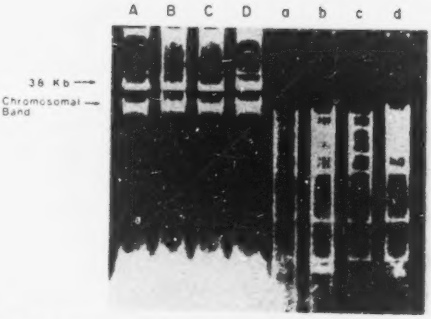

Figure 2. Agarose Gel Electrophoresis of Plasmids (Lanes A through D) and *Hind*III Endonuclease Restriction Fragments (Lanes a through d) Showing Identity of Human and Livestock *S. newport* Isolates from Minnesota and South Dakota.

Lanes A and a are from the South Dakota dairy herd, November 1982; B and b, from the owner of this herd, March 1983; and C and c and D and d, from two patients in the Minnesota outbreak, January through February 1983.

The beef cattle had been fed subtherapeutic amounts of chlortetracycline throughout 1982 for growth promotion and disease prevention, but no therapeutic concentrations of antimicrobials. The farmer added chlortetracycline to the feed by hand, approximately 100 g per ton (0.9 metric ton) of feed. All 105 head from this herd had been slaughtered in Minnesota in January 1983, and 59 carcasses were sent to Nebraska for processing into boxed beef (Fig. 1). (Boxed beef is usually sold to supermarket chains, which grind it into hamburger.) Of the other 46 carcasses, 12 could be traced to a vocational school in Minnesota that trained butchers; *S. newport* was not recovered from anyone in the area to which the vocational school supplied beef. On the day after the 59 carcasses had been cut and packed in boxes in Nebraska, 40,000 lb (18,000 kg) of boxed beef — which could have included meat from both the suspect herd and other herds — were sent to a meat-brokerage firm near Minneapolis–St. Paul. The boxes were traced through the computerized records of the meat broker to six to seven supermarkets named as the source of ground beef by the eight patients in the initial outbreak who lived in the Minneapolis–St. Paul area. Also, three days after the beef had been processed in Nebraska, 30,000 lb (14,000 kg) of "50:50 trim," which is also used for hamburger, were shipped to a meat-brokerage firm that supplied supermarkets used by Patients 5 (southern Minnesota) and 16 (Iowa) (Fig. 1).

We obtained and analyzed 91 nonhuman *S. newport* isolates from the National Veterinary Services Laboratories — 9 isolates from the six-state area in 1982 and the first half of 1983, and 82 isolates from throughout the continental United States from October 1981 through September 1982. Only the isolate from the dairy herd of Patient 4 had exactly the same antimicrobial-resistance pattern and plasmid profile as the isolates from patients in the outbreak groups (Fig. 2). Another 10 nonhuman isolates from Texas (two from swine and two from rabbits), Pennsylvania (three from cattle), Nebraska (one from cattle and one from swine), and Kentucky (one from a horse) had the same antimicrobial resistance and 38-kb plasmid as the isolates from the outbreak groups but also had a 5.1-kb plasmid and were resistant to sulfadiazine. These animal infections occurred before infection of the South Dakota dairy herd (November 1982) and the first cases of human infection (December 1982).

The 38-kb plasmid was not transferable by conjugation or transformation and could not be mobilized. The resistances shown by epidemic *S. newport* were not overcome by growth at high temperature or exposure to curing agents. However, plasmid DNA from the epidemic *S. newport* hybridized with the labeled DNA probe containing a gene sequence coding for beta-lactamase.

DISCUSSION

Our data indicate that multiply resistant *S. newport* caused serious disease in 18 persons in four states, 12 of whom had taken antimicrobials to which the organism was resistant. The patients took these drugs — in three instances without the direction of a physician — for nondiarrheal medical disorders such as pharyngitis and usually became ill within 24 to 48 hours after starting their medication. In addition to the rarity of pharyngitis and bronchitis as symptoms of nontyphoidal salmonellosis, their long duration in eight patients (average of eight days for pharyngitis and four days for bronchitis) before these patients took antimicrobials makes it unlikely that these symptoms were part of the prodrome of salmonellosis. Rather, the rapid onset of gastrointestinal illness after antimicrobial use suggested that most of these patients had an asymptomatic infection, and that the use of antimicrobials to which the *S. newport* was resistant constituted selective pressure that allowed growth of the organism. The histories of two patients — one taking penicillin for a week, and another having a cold for a week before the onset of salmonellosis — suggested that the converse also occurred — i.e., changes in gut flora preceded infection with resistant bacteria. Recent work by Riley et al. has shown that use of penicillin derivatives in the four weeks before salmonellosis is a significant risk factor for disease from resistant organisms.[13] This risk may result because antimicrobials allow the clinical expression of previously asymptomatic infections with resistant bacteria.

The number of cases of asymptomatic and mild infection with multiply resistant *S. newport* in these outbreaks is unknown, but it could be large since approximately 40,000 lb of potentially contaminated meat were distributed in the Minneapolis–St. Paul area. A previous study of *S. newport* transmitted in raw hamburger showed that an increased occurrence of salmonellosis in women 20 to 40 years old was associated with their tendency to taste hamburger before or while cooking it.[14] Although only two of the patients in our study admitted to this tendency, half the identified cases occurred in female food preparers, and food preparation alone may increase the risk of infection.[15] Although the meat distributed to the area may not have been uniformly contaminated, families of patients were likely to have eaten the same ground beef as the patients and may have been infected too. Among the 30 household contacts of Minnesota patients, only Patient 12 took antimicrobials; salmonellosis developed 48 hours after he had taken two capsules of amoxicillin used by his wife (Patient 6) six days before. Many people taking antimicrobials for common illnesses such as pharyngitis[16,17] may be at risk of serious illness if they are already inapparently infected with antibiotic-resistant enteric pathogens.

Epidemiologic and laboratory investigations suggested that the source of the resistant salmonella was a beef herd in South Dakota. Although suspect hamburger was not available for culture, the exposures of the ill persons in Minnesota, South Dakota, and Iowa coincided with the distribution of the meat. In addition, the only human (six-state area) or animal (United States) isolate of the epidemic strain of *S. newport* in the year before the outbreaks was from dairy cows on a farm adjacent to the farm of the beef herd.

The ultimate source of the R plasmid found in the epidemic salmonella strain is unknown. Analysis of *S. newport* from animals and human beings in the United States in the year before the outbreaks revealed the 38-kb plasmid, in association with other plasmids, in isolates from 10 animal populations in four states in 1981 and 1982 and one patient with infection acquired in Mexico or Texas in June 1982. Thus, the beef herd was probably not the original source of the R plasmid, but the use of subtherapeutic tetracycline in the herd's feed throughout 1982 provided a selective pressure for persistence of the antimicrobial-resistant organism.[18-20] Addition of antimicrobials to feeds at subtherapeutic concentrations to enhance growth of food animals is a common practice, and this use encourages not only the persistence of resistant bacteria but also the acquisition of resistance.[18-23]

Transfer of antimicrobial-resistant bacteria from animals to human beings under natural conditions is thought to be frequent but impossible to determine accurately.[8,9,24-26] Determination of all steps from farm to consumer is difficult because of the complex sequence of events from selection for resistant bacteria[18-23] to transmission in food[14,27] and ascertainment of resultant disease. The difficulty in documenting these events in sequence has been important in the controversy over antimicrobials in animal feed, since the lack of the kind of evidence shown in these studies has been cited by proponents of antimicrobial feed additives as demonstration of their safety.

Such complicated steps in transmission obscure the actual source of antimicrobial-resistant bacteria, as in institutional outbreaks that may actually derive from animal reservoirs.[28,29] In the outbreak that we have described, *S. newport* of animal origin apparently contaminated a sigmoidoscope, which may have been inadequately disinfected,[30] and eventually resulted in a fatal case of nosocomial salmonellosis. In addition, two household contacts of outbreak patients became ill long after the outbreak had ended, suggesting secondary spread from family members. These cases of apparent person-to-person spread were ultimately of animal origin, suggesting that controversy regarding the relative importance of person-to-person transfer of enteric bacteria as compared with animal-to-person transfer[7,31,32] may be based on an artificial distinction. Recent studies[33] corroborate our suggestion that sporadic cases of salmonella infection continue to occur after introduction of bacteria through contaminated meat products.

We conclude that antimicrobial-resistant bacteria of animal origin can cause serious human disease, especially in persons taking antimicrobials, and that the emergence and selection of such organisms are complications of subtherapeutic antimicrobial use in animals. We advocate more prudent use of antimicrobials in both people and animals.

We are indebted to the following persons for assistance in investigating the Minnesota cases: Karen E. White, M.P.H., Jack A. Korlath, M.P.H., and Joel N. Kuritsky, M.D. (Acute Disease Epidemiology Section, Minnesota Department of Health), Darwin E. Zaske, Pharm.D. (St. Paul–Ramsey Medical Center), John M. Lanier (Minneapolis Center for Microbiological Investigations), John Feldman, Jeffrey Spykerman, David Yost, and Gary Quam (Minneapolis Office, U.S. Food and Drug Administration), and John G. McCullough, B.A., and Juanita E. Heiser, B.A. (Minneapolis Department of Health).

We are also indebted to Bob Cooksey, Ph.D., and Nancy Clark, M.S. (Antimicrobics and Infectious Mechanisms Branch, Centers for Disease Control), for performing DNA hybridization between the R plasmid and their labeled probe; to Janice Haney, B.S., and Joy Wells, M.S. (Enteric Bacteriology Laboratory, Centers for Disease Control), and Mr. David Janssen (Wisconsin State Hygienic Laboratory) for testing isolates for antimicrobial susceptibility; to Kris Birkness, B.A., for performing preliminary plasmid analysis of isolates from some outbreak cases; and to Billie Blackburn, D.V.M. (U.S. Department of Agriculture, Iowa) for supplying all nonhuman *S. newport* isolates.

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Health Promotion Awards – Continued

Full descriptions of the programs are available from the respective state health agencies; a publication describing the Secretary's Health Promotion Awards Program and the awards for 1986 will be available in July from the Center for Health Promotion and Education, CDC; descriptive abstracts of all 197 projects are currently available in the computerized Combined Health Information Database on BRS Information Technologies.

Reported by the Div of Health Education, Center for Health Promotion and Education, CDC.

Editorial Note: The Secretary's Community Health Promotion Award was established in 1982 to recognize exemplary local community and state efforts to improve the health of their citizens. In addition, explicit identification of successful community projects promotes them as models for efforts in other communities. Projects aimed at risk reduction for chronic diseases, injuries, infant mortality, and others are eligible and have been recognized in the past. Criteria for award include documentation of evaluation of impact on the selected health problems. Interested agencies should contact the community health agencies identified here regarding specific projects or the respective state health department regarding the Secretary's Community Health Promotion Award process.

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Morbidity and Mortality Weekly Report
Centers for Disease Control, USPHS - DHHS
June 27, 1986

Epidemiologic Notes and Reports

Bacteremia Associated with Reuse Of Disposable Hollow-Fiber Hemodialyzers

Since May 6, 1986, CDC and the U.S. Food and Drug Administration (FDA) have received reports from four free-standing hemodialysis clinics of clusters of patients with gram-negative bacteremia. These patients were undergoing maintenance hemodialysis at clinics in which disposable hollow-fiber hemodialyzers were reused on the same patient after disinfection with a recently introduced chemical germicide, RenNew-D (manufactured by Alcide Corporation, Norwalk, Connecticut, and solely distributed by Cobe Laboratories, Inc., Lakewood, Colorado).

CDC and FDA have participated in investigations of these clusters at two of the four clinics. A total of nine patients at these two clinics met a case definition of intradialytic sepsis based on the following criteria: (1) absence of signs or symptoms of infection at the initiation of the dialysis session; (2) presence of one or more of the following signs or symptoms during the dialysis session: shaking chills, fever, hypotension, nausea, vomiting; and (3) growth of gram-negative microorganisms from blood cultures obtained during or following the dialysis session. Review of microbiologic records in these centers showed no clusters of gram-negative bacteremia during the preceding 6 months. All the patients were treated with parenteral antimicro-

Bacteremia — Continued

bials and recovered without apparent sequelae. Microorganisms isolated from the blood cultures included *Pseudomonas aeruginosa* (five patients), *P maltophilia* (three), *Acinetobacter calcoaceticus* (var. lwoffi) (three), *P. putida* (one), and *Alcaligenes denitrificans* (one). Three patients had two or more microorganisms isolated from their blood. These two hemodialysis clinics had been using RenNew-D for reprocessing of hemodialyzers for 6 weeks and 4 months, respectively, before the first documented case of bacteremia.

Microbiologic investigation of hemodialyzers at one of the four clinics showed bacterial contamination of the blood compartment in 10 of 20 hemodialyzers after reprocessing with RenNew-D during the week of June 9. For the 17 hemodialyzers for which the number of reuses was documented, the number of previous uses ranged from one to 50. Changes in the mixing and handling of RenNew-D were subsequently made by the staff at the hemodialysis clinic after consultation with representatives of the manufacturer and distributor of the product. Following these changes, cultures were performed of: (1) RenNew-D drained from stored reprocessed hemodialyzers; (2) saline that had been used to rinse the blood circuits, including the interiors of reprocessed hemodialyzers and other components of the blood circuits, before dialysis; and (3) blood obtained from the blood circuit during the patients' dialyses. Gram-negative microorganisms were identified in none of 137 samples of RenNew-D, in seven (6%) of 108 samples of the predialysis saline rinse, and in blood cultures from 11 (11%) of 102 patients.

It has not been determined why hemodialyzers showed evidence of contamination after reprocessing with RenNew-D. The manufacturer has initiated a voluntary recall of all lots of the product. Studies are in progress to evaluate the source and possible causes of these clusters.

Reported by GT Flynn, Community Dialysis Svcs, Inglewood, SH Waterman, MD, Los Angeles County Health Dept, SB Werner, MD, California Dept of Health Svcs; TF Parker, MD, Dallas Kidney Disease Center, G Green, MD, CE Haley, MD, Dallas County Health Dept, CE Alexander, MD, State Epidemiologist, Texas Dept of Health; Center for Devices and Radiologic Health, US Food and Drug Administration; Hospital Infections Program, Center for Infectious Diseases, CDC.

Editorial Note: The practice of disinfecting and reusing hemodialyzers labeled "for single use only" has been adopted by more than 50% of hemodialysis centers responding to surveys of dialysis-associated diseases (*1*). Bacterial contamination resulting in patient infections has previously been documented in hemodialyzers that were reprocessed with benzalkonium chloride (*2,3*) and 2% formaldehyde (*4*).

Until further information is available, CDC recommends that providers of hemodialysis services review their experience and assess the clinical safety of their hemodialysis practices. Evaluation of reuse programs should include active surveillance of hemodialysis patients for both infectious and noninfectious complications. Clinical, laboratory, and epidemiologic information about patients experiencing adverse reactions should be recorded in the patient's medical record, as well as in a log book, so that incidence rates of these complications can be determined. Additional studies of the functional and microbiologic quality of reprocessed hemodialyzers, as well as the factors affecting their clinical safety, are needed to formulate guidelines.

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Senator SARBANES. Thank you very much. Next we'll hear from Ms. Elaine Larson, the holder of the Nutting Chair in Clinical Nursing.

STATEMENT OF ELAINE LARSON, R.N., PH.D., F.A.A.N., NUTTING CHAIR IN CLINICAL NURSING, JOHNS HOPKINS UNIVERSITY

Ms. LARSON. Thank you, Mr. Chairman, members of the subcommittee, and other participants.

The world of hospital infection control is rather small, so it's a pleasure for me to join my colleagues here today to discuss one vital aspect of our field, that of disinfection and antisepsis.

My expertise does not lie in the area of environmental disinfection, but rather with antisepsis: the application of cleansing agents to living tissue.

As has been clarified previously, since antiseptics come in direct contact with human skin, they lie within the preview of the Food and Drug Administration rather than the EPA.

I would support what my colleagues have been saying, that we consider the possibility of having chemical disinfectants and antiseptics under the same regulatory body. However, what I would like to do is draw some parallels between the problems at the EPA and the FDA, and, frankly, right now just moving the testing and standardization of chemical disinfectants from EPA to FDA would not solve the problem.

For the past 8 years I have been conducting research on skin antisepsis, particularly handwashing, and I appreciated your comments, Congressman Scheuer. We've done five or six studies, as a matter of fact, on how often health care personnel wash their hands before they contact patients, and let me say that it is very sad—it's another problem, but all the more reason that we need antiseptics that work when people do wash their hands. We have found, and others, in various studies, that people wash their hands—physicians, as little as 17 percent of the time between examining patients in private offices. And even in hospitals, this is under observation, when in many cases when people even are aware that they are being observed. In hospitals we found that less than 50 percent of times, after touching patients with known infectious diseases, are hands being washed. These statistics are from studies that have been published.

My studies have been sponsored by industry, through my academic affiliations, and by grants from private and public agencies. As a result of this work, my collaborators and I have come to appreciate the seriousness of the need for three things. First of all, standardization with regards to protocols for testing of antiseptic and disinfectant products. Second, identification of criteria for minimum acceptability of tested products. Even when we have standard testing methods, what defines whether or not a product is, indeed, safe and effective? And, third, a clear delineation of who is responsible for such standard setting, and for deciding when and how an antiseptic or a disinfectant should be used.

For almost a decade, there has been essentially no direction from any government agency regarding acceptable test standards or criteria for choosing appropriate and effective agents. In 1978, in the

Federal Register, was published the proposed rules for testing antiseptics, and to my knowledge these are still proposed rules. To complicate the matter, the Centers for Disease Control, which published guidelines considered to be the "gospel" of infection control practice, has equivocated in their 1986 Guideline for Handwashing and Hospital Control. This guideline gives minimal direction regarding what kinds of soaps to use and how much soap should be used. They state that they cannot recommended the use of antiseptics for handwashing by health care personnel because of lack of randomized controlled clinical trials to demonstrate the effectiveness of antiseptic handwashing on decreasing hospital-acquired infections.

We need these studies. If we find, for example, that personnel handwashing with antiseptics has little or no effect on the rate of hospital infections, then hospitals across the country can drastically curtail their use of antiseptics, saving hundreds of thousands of dollars every year. On the other hand, if we find with such studies that when physicians and nurses wash their hands with an antiseptic soap, the incidence of infections is reduced, we can put a dent in the multimillion-dollar problem of hospital infections.

Regardless of the findings of such studies, if we find out that antiseptic soap helps or not, we can't lose. Without these studies, however, we are making decisions about patient care without adequate knowledge of what is safe or effective.

The irony is that as long as the Government chooses to take a passive role in the evaluation of antiseptics and disinfectants, such trials will not be conducted for two reasons: First, industry, understandably, will not do expensive research if it's not required; second, it's extremely difficult to get any funding agency to support such sophisticated and costly studies when the Government, by virtue of the fact that they are not taking a stand on the issue, implies that such studies are important.

For example, I currently have a grant resubmitted under review at the National Institutes of Health for just such a randomized clinical trial of the efficacy of antiseptic handwashing and infection control. But I have little hope that it will be funded, even if the study design is excellent and the potential value is there, because of the priorities at NIH.

I would like to just show you a few slides.

[Slide.]

This is a red fluorescent dye placed on the gloved hands of attendants. It is invisible to the naked eye when it's put on. It only shows up under certain kinds of light. And such devices are used to trace, for example, where the hands contact various things.

[Slide.]

You can see this is actually in a dental lab. Some of the areas that are contacted by the hands, you can imagine what a patient would look like if we took a picture of a patient after they had been handled by such hands.

This is during handwashing, of course. As I said, people who have the dye on can't see it so they don't know what they are doing and we are looking at the traces of the dye, as a substitute for organisms.

Representative SCHEUER. Excuse me, that dye——

Ms. **Larson**. This is fluorescent dye on the hands that's placed on there: It's not visible except under certain light. This is just a demonstration of what is touched by the hands.

[Slide.]

So you can see even after handwashing there's still dye left on the sink, for example.

[Slide.]

These are organisms that grow on various pieces of equipment. This, for example, is a dental chair and some chair buttons.

[Slide.]

These are some culture plates which are organisms taken from some of our studies from the hands of health care personnel after handwashing, immediately after handwashing. The plate on the left is after handwashing with a plain soap. The plate on the right is after handwashing with an antiseptic. Of course the skin can never be sterilized so you always find organisms, which is why surgeons, for example, wear gloves.

And this is just a picture taken on a hospital unit. I went around and collected the various soaps that were available for health care personnel on the unit, put them at one sink, and you can see the confusion that health care personnel have with the various soaps that are available for their use. Some are antiseptics, some are plain, some liquids, some bars. All of them are categorized as over-the-counter category III agents, which means that none of them have been tested for—have adequate testing for safety and efficacy.

The reason they are all category III is because basically there's no testing so, right now, no product can move with much ease from category III that is not proven to be safe and efficacious, to category I, which is demonstrated to be safe and efficacious.

The essential issue, then, is really an individual one. If you were a patient about to undergo a potentially dangerous invasive medical procedure, would you want your health care attendants to wash their hands thoroughly with an antiseptic? And, would you want to be assured that any instruments used were disinfected with an agent that had been thoroughly tested for safety and effectiveness?

Dr. Guess, former chair of the FDA Over-the-Counter Topical Antimicrobial Review Panel, stated he would be upset if he found his physicians and nurses washed their hands with only soap and water, despite the fact that this is the CDC recommendation at this time. Again, FDA, EPA, and CDC insist on taking a passive role on decisionmaking regarding this essential aspect of patient protection.

I strongly urge you, as one important step toward solving this problem in the prevention and control of infection, to consider reopening the EPA lab for testing of disinfectants and possibly to consider in the future the idea of having antiseptics and disinfectants under the same regulatory body. Thank you.

Senator **Sarbanes**. Thank you very much, for a very lucid presentation. Mr. Rutala, please proceed.

STATEMENT OF WILLIAM A. RUTALA, PH.D., RESEARCH ASSOCIATE PROFESSOR, UNIVERSITY OF NORTH CAROLINA SCHOOL OF MEDICINE; AND CHAIRMAN, GUIDELINES COMMITTEE, ASSOCIATION FOR PRACTITIONERS IN INFECTION CONTROL

Mr. RUTALA. Thank you. My name is Bill Rutala. As a researcher in the area of disinfection and practitioner in infection control, I want to thank you for the opportunity to be here and discuss the important issue, testing of hospital disinfectants.

In Joseph Lister's presentation before the British Medical Association in 1867, he referred to the positive influence that antiseptic treatment has "upon the general healthiness of a hospital." Now, 119 years later, we have innumerable chemical disinfectants and antiseptics to help us achieve that state of healthiness by reducing microbial contamination of the animate and inanimate environment to a level unlikely to allow transmission of infection. For this reason, the germicidal activity of disinfectants—used to decontaminate patient care supplies or equipment—and antiseptics—used to decontaminate skin and other superficial tissues—may be the most important criterion for selecting a particular germicide.

While neither disinfectants nor antiseptics are required to sterilize treated objects, they should not support bacterial growth in stock or recommended use-dilutions, and should meet their germicidal label claims. Such, however, is not always the case, as articles in the infection control literature emphasize.

Contaminated or ineffective disinfectants and antiseptics have occasionally caused hospital infections for more than a quarter of a century. What is disinfection and when would a contaminated or ineffective disinfectant most likely be the cause of hospital infections? Can hospitals and other users be sure that disinfectants meet their germicidal label claims? What control measures could be instituted to prevent recurrence of these products as the source of hospital-acquired—nosocomial—infections? These are a few of the questions that will be addressed in my comments.

I should also mention that henceforth, my comments will be restricted to the topic of this hearing, hospital disinfectants, but contaminated or ineffective antiseptics used in the health care setting have been equally, if not more, problematic.

For example, there are at least 23 published reports of contaminated antiseptics. Nosocomial infections have been commonly associated with contaminated antiseptics, principally when these agents were used for direct patient care activities such as wound and skin care or as a skin preparation before invasive procedures.

What is disinfection? Disinfection is an intermediate process between cleaning and sterilization. The objective of disinfection is to prevent infection by reducing microbial contamination on inanimate objects to a level unlikely to be hazardous. This may be accomplished by steam and gas sterilization, wet pasteurization, and chemicals.

The categories of disinfection are based upon the degree of infection risk involved in the use of the item. The three categories of risk of patient care items are critical, semicritical, and noncritical.

Critical items are so called because of the high risk of infection if such an item is contaminated with any microorganism, including bacterial spores. Items in this category—for example, surgical instruments, cardiac and urinary catheters and implants—enter sterile tissue or the vascular system and must be sterilized. Since most of the items in this category are purchased as sterile or sterilized by steam or gas sterilization if possible, chemical sterilization is not commonly employed.

Semicritical items will come in contact with mucous membranes or skin that is not intact, and must be free of all microorganisms with the exception of bacterial spores. These items—for example, respiratory therapy and anesthesia equipment, and gastrointestinal endoscopes—minimally require high level disinfection, using wet pasteurization or chemical germicides.

Noncritical items such as floors, walls, bedpans, crutches, and patient furniture in a hospital setting come in contact with intact skin and require low level disinfection.

When would a contaminated or ineffective disinfectant most likely be the cause of hospital infection? It is when critical and semicritical patient care items which have been inadequately disinfected come into contact with sterile tissue, mucous membranes, or skin that is not intact. In fact, most of the reports that describe illness associated with contaminated or ineffective disinfectants used the products to disinfect direct patient-care items, such as cystoscopes, cardiac catheters, and thermometers. Contaminated noncritical patient-care items have rarely been associated with hospital-acquired infections.

Can hospitals and other users be sure, today, that disinfectants work as they are supposed to? No. In August 1985 through January 1986, Dr. Gene Cole and I conducted a collaborative study of the AOAC use-dilution method to assess interlaboratory variability of results and set specifications for pass/fail. This study also allowed us to examine the manufacturers' claims of germicidal activity against the AOAC-recommended test bacteria, Staphylococcus aureus, Pseudomonas aeruginosa, and Salmonella choleraesuis. The former two bacteria are common nosocomial pathogens.

Eighteen laboratories in the United States participated in this collaborative study. These laboratories represented disinfectant manufacturers, independent testing facilities, and Federal and State laboratories. Each of the participating laboratories received six aliquots of concentrated hospital disinfectants—three phenolics and three quaternary ammonium compounds—as supplied by the manufacturer. The randomly selected products were not identified by brand name and the laboratories were asked to process each disinfectant—at its stated use-dilution concentration in distilled water—by performing use-dilution tests as normally done in their laboratory.

Table 1 in my handout presents an overview of how the disinfectants performed.

Most laboratories, 80 percent, passed the test disinfectants when challenged with Salmonella choleraesuis. However, only 66 percent and 38 percent passed the test disinfectants when challenged with Staphylococcus aureus and Pseudomonas aeruginosa, respectively. Three of four manufacturers' laboratories unknowingly tested and failed their own product.

It is apparent from this large collaborative study that some disinfectants do not meet the products' claim of germicidal activity against bacteria. What is not apparent from the information I have presented thus far is the enormous interlaboratory variability in results.

It can be seen in table 2 in my handout that some laboratories failed all of the products: for example, laboratories Nos. 3, 17 and 18; and a failure is greater than 1 positive penicylinder per 60; while other laboratories passed most or all the products: for example, laboratories Nos. 5, 7 and 13.

Of particular concern is the situation where a disinfectant, No. 6, failed in 14 laboratories yet passed in 4. This interlaboratory variability in results is largely attributable to the 20 or so presumed or known deficiencies in the use-dilution test. This variability in test results, among laboratories testing identical products, questions the use of the AOAC use-dilution test for enforcement action.

Currently, an EPA and University of North Carolina cooperative agreement provides for the investigation and subsequent revision of the present AOAC use-dilution test.

What control measures should be instituted at the Federal level to reduce the frequency of contaminated or ineffective disinfectants and the threat of serious nosocomial infections related to their use? Manufacturers' efficacy claims against microorganisms should be verified by an independent laboratory or by the appropriate Federal agency—which is EPA for disinfectants—using a standardized test. The preregistration testing of disinfectants should not commence until there is a test which eliminates variability in the methods used and results obtained.

Hospital laboratories should not be expected to conduct the AOAC use-dilution test because of cost, methodological nuances, and redundancy. Preregistration efficacy testing of disinfectants using a standardized test would provide assurance that disinfectants meeting the requirements are capable of achieving a certain level of antimicrobial activity when they are used as directed. Unless control measures are instituted, one can confidently predict that additional reports will emerge that describe contaminated or ineffective disinfectants and nosocomial infections secondary to their use. Thank you very much.

[Tables 1 and 2 referred to by Mr. Rutala follow:]

TABLE 1 Results of AOAC Use-Dilution Collaborative Study

Organism	*%Pass**
Salmonella choleraesuis	79.6% (86/108)
Staphylococcus aureus	65.7% (71/108)
Pseudomonas aeruginosa	38.0% (41/108)

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*Number of AOAC Use-Dilution tests (60 carriers/test) passing out of 108 (108=18 laboratories testing 6 unknown disinfectants).

Table 2. Use-Dilution Method Collaborative Study Results for *Pseudomonas aeruginosa*

Lab	Number positive tubes/60 Disinfectants 1	2	3	4	5	6
1	15	9	6	1	1	52
2	1	0	0	0	0	16
3	14	8	11	2	4	13
4	7	1	2	0	0	22
5	0	0	0	0	0	2
6	4	7	3	3	0	1
7	1	1	1	1	0	1
8	7	3	4	3	0	40
9	6	5	0	2	5	18
10	10	1	0	0	1	7
11	5	2	0	2	4	2
12	8	5	1	1	0	58
13	1	2	1	1	0	1
14	3	3	2	3	2	1
15	8	8	10	2	0	5
16	10	8	3	2	0	6
17	60	59	59	56	26	59
18	10	15	3	11	4	5
Pass (0, 1/60)	22%	28%	44%	44%	67%	22%
Fail (>1/60)	78%	72%	56%	56%	33%	78%

Senator SARBANES. Thank you very much, Mr. Rutala. I want to thank all the members of the panel for the very high quality of their statements. They are very helpful to the committee and we appreciate it very much.

I have just three brief questions. The Senate actually is going to go into a series of votes sometime between 11:30 or 12:00. In fairness to the next panel, I want to try to move things along a little.

First of all, Ms. Larson, what was your figure on the people who just didn't bother to wash between their activities? Was it 50 percent?

Ms. LARSON. The lowest figure is from a study that was done in Europe. Actually we didn't talk about differences in infection rates in other countries, which I'm sure we all could comment on if we had time.

Senator SARBANES. Why don't you take a second and do that, because Congressman Scheuer asked about that.

Ms. LARSON. Dr. Gröschel may have some comments, too. My impression is that there is much more emphasis in Europe on environmental disinfection and skin antisepsis than there is here and there has been for a long time. Whether or not there's really a difference in infection rates is another question that I don't think—maybe some of us can answer. I probably can't. I don't think they are really different. I think that we may have differences in reporting mechanisms.

What do you think about it, Dr. Gröschel?

Dr. GRÖSCHEL. I think it is mainly due to the surveillance programs which have been instituted. Whereas in the United States the surveillance programs are highly centralized, in Germany where I am very familiar, the programs are not as well developed throughout the country, but more regionalized or individualized. I would say that the nosocomial infection rate in Europe is not any different than here. But, again, it depends on the size of the institution and the type of institution.

Ms. LARSON. But just to briefly answer your question, the lowest rate of handwashing I've seen in a published study of observed data was 17 percent of the time that private physicians, between examinations of patients, they wash their hands. That was not a study that we did here. That was in Europe.

In our studies, as I said, we have done, now six observational studies during which some of the health care workers knew they were being observed and knew their behavior was being observed for handwashing and other times they didn't. It didn't make any difference if they knew they were being observed or not. The average is between 35 and 50 percent of the time that a handwashing should occur, that is they are contaminated. Does it indeed occur, that's another issue.

Senator SARBANES. As you say, let's test and find out. If we find out that it is helpful and would work, then we are in a better position to put the pressure on for it to be done.

So long as there's some doubt about all of that, as there currently is, most people say: Well, you know, it doesn't make any difference anyhow. They are not going against an established standard.

Ms. LARSON. Two comments. One is, I think you are absolutely correct. Health care workers do not always believe that handwashing does, indeed, affect nosocomial infections. We have evidence from Semmelweis that it does, but we don't know how often it should occur. The other comment is there's a belief among health care workers that if one washes with an antiseptic, one does more damage to the skin. In studies that we have done with antiseptic versus control soap—that is, Ivory, Dial, nonantiseptic soap—there's no difference in damage to the skin. The damage to the skin occurs with all handwashing, it's true. We need the minimum amount of handwashing that is necessary to reduce infections and no more, but certainly not any less. That's what we need tested.

Senator SARBANES. Does anyone else want to add anything? Then let me go to my second question.

This involves the effort to determine costs, of course, which is allegedly underway now in the administration. I don't think they do very accurate cost-benefit analyses, but let's assume that that's the context in which we are going to view this issue. I have never been prepared to accept that in the health care field, because I don't think you can simply frame the question in economic terms when people's health and lives are at stake. But let's just take the economic argument.

Would you say that the savings realized by the higher efficacy of disinfectants, which could be assured by a more effective and comprehensive testing program, would offset the additional cost of the testing program? And, if so, do you have any estimate of the order of magnitude?

Dr. SCHAFFNER. Senator, that's an excellent question. You can see, none of us are rushing to the microphone. One would certainly expect that that would be the case, but I have seen no careful calculations to the point.

Ms. LARSON. There was a study just done by the Centers for Disease Control, the "Study on the Efficacy of Nosocomial Infection Control," the SENIC study, and based on that date, if anything reduces the risk—for example, the surveillance mechanisms that we have now reduces nocosomial infections by as little as 6 percent—it pays for itself.

We did a cost-benefit analysis in the grant we submitted to NIH and we found that either way, if we find out that antiseptics work and reduce infections by as little as 5 percent, we save money. And, if they don't work, then we can stop using them, and save money. The only difference is that if we have testing, we will have a systematic way of finding out what works. Right now we don't have a systematic way of finding out what works. I think it's cost effective.

Senator SARBANES. Yes, sir, Dr. Gröschel.

Dr. GRÖSCHEL. I think Senator Gore pointed out before that we do know about certain incidences which are reported in the literature, where disinfectants or antiseptics failed. But we do not have good information on the individual patient who develops nosocomial infection, what was necessarily the cause-effect relationship between the use of disinfectants and antiseptics, and the nosocomial infection. I think Dr. Schaffner will probably support my statement.

Senator SARBANES. I would just observe that one of the difficulties is that we don't do overall social budgeting. In other words, if the EPA stops its lab, then the EPA reflects a saving in its budget.

The subsequent costs associated with the EPA when the lab is closed are not reflected in the EPA budget. Those costs take place out in the society. They are paid for by a patient in a hospital, or by the hospital itself, in some way or other. In effect, those costs are real but they are never put on the same balance sheet in order to set them off, one against the other, so that a direct comparison is possible. And I agree with Ms. Larson that the degree to which it would have to be effective in percentage terms, in order to more than cover the costs of the testing program, is not very great. The costs of the testing program are not very high, as a matter of fact.

Mr. Rutala.

Mr. **Rutala.** Yes, sir. I think to substantiate what you are saying, the cost to perform germicidal efficacy testing has been estimated to be approximately $500,000. If one considers momentarily that the average nosocomial infection costs $2,000, one would only need to prevent roughly 250 nosocomial infections by performing the germicidal efficacy test for both disinfectants and antiseptics to be at least cost effective.

Senator **Sarbanes.** Congressman Scheuer.

Representative **Scheuer.** Well, I wish to reiterate what Chairman Sarbanes has said. This was an exceptionally fine hearing, with four really truly outstanding witnesses. Rarely do we get the consistent extraordinary quality of testimony. I don't want to seem a Pollyanna, but it was a marvelous experience listening to you all.

The Centers for Disease Control in Atlanta does publish experiences of nosocomial infections, comparative figures as between hospitals. Has anybody ever done an analysis as between hospitals with high rates of nosocomial infections and hospitals with low rates, as to whether that is caused by carelessness or simply not using the available antiseptics and disinfectants? Or whether much of it or most of it is caused by inadequate and nonworking antiseptics and disinfectants? Or is it both of the above?

Dr. **Schaffner.** That question has been looked at, Congressman. The major determinants that result in different nosocomial infection rates between hospitals has to do with the population of patient care by the hospital. Small community hospitals take care of, relatively speaking, not very complicated patients. Those patients are sent to the more complicated medical centers, where those institutions have then—of course the patients have a variety of severe underlying illnesses and the therapeutic interventions are much more elaborate. We have a much higher nosocomial infection risk.

Representative **Scheuer.** In the tertiary hospitals?

Dr. **Schaffner.** In the tertiary care hospitals, yes. That's far and away the major determinant.

Representative **Scheuer.** Wouldn't a lot of that also be caused by the fact that these patients so frequently involved have a reduced and far less effective immune system?

Dr. **Schaffner.** Exactly. That's part of the gross problem the patients have. Yes, indeed.

Now, I think the issue of what proportion of infections that occur, both in the tertiary care center and in the community hospital, could be reduced if we had more effective disinfectants and antiseptics is still an open issue. But as my colleagues have said, you wouldn't have to reduce those percentages very much in order to make this a cost-effective program.

Representative SCHEUER. Yes. We do have ways of valuing the worth of a human life. The Government has put out statistics that smoking causes the taxpayers approximately $60 billion a year; about $25 billion due to direct health costs in hospitals; sickness costs. And the other $35 billion in death costs: losses from work and so forth. So we do have a sort of—and I think the actuaries know how to figure the loss of a life, airplane accident deaths. I can't believe any rigorous cost-benefit analysis wouldn't show a spectacular cost-benefit analysis from the very modest order of magnitude of investments here. I couldn't agree with you more.

One last question because I know that we are all impatient to get on to the next panel.

Dr. Gröschel, you asked a question in your statement. Who is responsible to the public to assure the efficacy and the label claims of chemical disinfectants and sterilizers? Well, let me just say, I think the public is a little bit result oriented here. They aren't so much interested in what brands the hospital uses. What they are interested in is which hospitals are dangerous to their health and which hospitals have a much higher rate of nosocomial infections than other hospitals. As between tertiary hospitals or as between primary hospitals.

Can you think—do you think it would be justifiable for our government to consider ways of giving information to health care consumers—that is, we the patients of America—comparative information on hospitals that would be intelligible to them? Not a scientific monograph but some guidance like—the patient—it is over in Canada——

Dr. SCHAFFNER. Patient package insert?

Representative SCHEUER. Patient package insert, in the type of language you could understand and the kind you could understand. I can't read patient package inserts without my glasses and even then I have to peer and agonize.

Would it be a useful function of government to give intelligible, simple indications of which hospitals, historically, from experience, have a high rate of nosocomial infections and which hospitals, due to a high rate of personal effort on the part of staff, perhaps care in picking the disinfectants and sterilizing agents, have had a more successful rate in controlling nosocomial infections? Would that be a useful thing for the Government to do? To help consumers make these incredibly important choices as between health care deliveries?

Dr. GRÖSCHEL. I would like to make just a personal comment, not for the ASM. I don't think this is possible. It is not possible because of the things we have mentioned before, the composition of patient populations in different institutions. Having been associated with a cancer institution in Texas for a number of years where we had patient infection rates of 120 percent in a leukemia service, versus a few percent only in other areas—for example, skin cancer patients—I think this would give the population a false piece of information. Because, my institution, which is a tertiary care institution or a cancer institute with 15 percent infection rate, would look very bad and it would intimidate my patients to go to this institution.

Represenative **Scheuer**. Let me clarify that. The CDC does put out information. They published a chart that was published in the New York Times about 6 or 8 months ago, and they have expected rates of nosocomial infections. And Kettering Memorial, Sloan Kettering, which you would predict to have a very high rate, had a much less than expected rate. And most of our primary hospitals around New York had a much higher rate. In other words, they can factor.

When you have terminal cancer patients whose immune systems have obviously deteriorated tragically and pathetically to the vanishing point, they would be much more vulnerable and of course those were factored into the figures that CDC put out. And they did give most of the tertiary hospitals around New York a rating that indicated they had significantly less than the expected rate of nosocomial infections and it was the primary hospitals that had comparatively well patients, with not very complicated diseases, with comparatively unimpaired immune systems in most of those patients, that had the higher than expected rates of nosocomial infections. So you raise a very valid point. But the CDC certainly had recognized in the way they put out comparative statistics. But it's not made available to health consumers. I was wondering if you thought that might be a valid goal. But I don't want to continue this. I have used up my time and we have another panel to get to.

Senator **Sarbanes**. Why don't we hear the response to that before we conclude. I don't want people to walk away saying: I wish I had a chance to say something.

Dr. **Schaffner**. I didn't wish to prolong it if you didn't wish to.

Representative **Scheuer**. Oh, I wish.

Dr. **Schaffner**. Congressman Scheuer, it's first of all an extremely desirable goal. Second, point of perhaps clarification, I believe those data came from Medicare and were not released by the CDC. Third, I think that it still is, despite—I can differ with you slightly—it is very difficult to factor in precisely the different kinds of patients that are in the hospital and then the data that are released on the hospital itself. If you would consider for a moment, if the hospital thought that its hospital-acquired infection data were going to be released, I believe that the intensity of surveillance would diminish. The harder we look in our hospital, the more infections we find. We have chosen a level of surveillance that we think let's us do our job very well. I believe that, as with the confidence that I have in my hospital administrator, if that good man thought that his data were going to be compared on the front page of our local paper, I might receive a little less support next year for my activities.

Representative **Scheuer**. In other words, that would be exactly the opposite result than one would hope to achieve.

Dr. **Schaffner**. I would think that might be an inevitable result, sir.

Representative **Scheuer**. Thank you very much.

Senator **Sarbanes**. We again want to thank this panel. You have been extraordinarily helpful. Will the next panel come forward.

I understand, Mr. Engel, you are accompanied by Mr. Eitzen, and we are very happy to have him with us as well.

Why don't we start with Mr. Carl Shaffer, the former Director of the EPA Laboratory at Beltsville. Pleased to have you here, sir.

STATEMENT OF CHARLES H. SHAFFER, FORMER DIRECTOR, EPA LABORATORY, BELTSVILLE, MD

Mr. **Shaffer**. My name is Charles H. Shaffer and I reside in Rockville, Maryland. I'm happy to have this opportunity to make a statement before this committee on behalf of the testing of hospital disinfectants.

I am a microbiologist by training and experience. My professional experience as a bacteriologist extend from 1942 when I was employed in the Bacteriology Division of the Food and Drug Administration, FDA, and later with the Division of Antibiotics in that same agency.

In 1963, I joined the Microbiology Laboratory at Beltsville, Maryland, which, along with other biological and chemical labs, was an integral part of the Pesticide Regulation Division, PRD, of the Department of Agriculture's Agricultural Research Service. That's ARS.

At that time the USDA administered the Federal Insecticide, Fungicide and Rodenticide Act known as FIFRA, prior to the creation of the Environmental Protection Agency in December 1970.

The EPA absorbed the Pesticide Regulation Division and assumed administration of FIFRA. Upon the retirement of the then-laboratory supervisor, Mr. Louis F. Ortenzio, in 1971, I became lab supervisor. I retired from the Government service in August 1978.

Under FIFRA, the agency, EPA, is given the authority to regulate pesticidal products. Included in this area of responsibility are the registration and compliance monitoring, sometimes referred to as surveillance, of pesticidal products. Antimicrobial products used on inanimate surfaces are considered pesticides under the law.

Of particular interest to this discussion are those products intended to eliminate and control disease-causing microorganisms. Products characterized as germicides, disinfectants, sanitizers, sterilants, virucides, fungicides, tuberculocides are examples. The target pests of these products are microscopic organisms, invisible to the unaided eye, such as bacteria, fungi, and viruses. The kinds and numbers of human diseases caused by microorganisms are extensive and, as can be seen in the periodic reports of outbreaks of one kind or another, or in the appearance of some hitherto unknown diseases, seemingly limitless. Such well-known diseases as influenza, tuberculosis, typhoid, or food poisonings are still very much with us.

Originally, the function of the Microbiology Lab was to perform efficacy testing of products for which any antimicrobial activity was claimed. This included a diversity of products such as: treated materials, carpet shampoos, fabric sanitizers, bathroom cleaners, swimming pool disinfectants, hospital disinfectants, dairy sanitizers, portable water purifiers, to name a few.

Since the mid-1970's, the scope of testing was narrowed down mainly to those products directly associated with maintaining public health: disinfectants and sanitizers used in hospitals, dental and other health care facilities, dairies, restaurants, barber and beauty shops, morgues and mortuaries. In order for public health related products to be registered, the manufacturer or registrant must present laboratory data to the agency attesting to its efficacy. These one-time data are developed by the registrant or for the registrant.

Preregistration or confirmatory testing done at Beltsville was for sporicidal and sterilizing products. These are the most demanding testing required of products for which cold sterilization claims are made. Such products would be used on surgical, optical and dental instruments and certain types of stationary equipment.

As part of the compliance monitoring enforcement program intended for the use of germicides, disinfectants, sanitizers, tuberculocides, fungicides and virucides were evaluated for effectiveness according to the label claims. Samples collected in channels of trade by EPA inspectors were sent to the Beltsville laboratories for chemical analysis, user safety and efficacy testing. The chemical analyses of the samples were strictly confined to determining the level of the principal active ingredients. In our experience, the vast majority of biologically failing samples did not contain the specified level of the active ingredient. It was readily obvious that with antimicrobial products, which are formulations of up to five or six ingredients, chemical analysis alone was not appropriate in judging the efficacy and safety of the product.

It is interesting to note that most, if not all, failing samples were registered products for which efficacy data was presented to the Agency in support of their registration.

The testing of disinfectants and related products are done according to the methods of the Association of Official Analytical Chemists, better known as the AOAC. Some of these methods were originally done at Beltsville. They have been used for many years as official test methods. I understand that there are current efforts in improving them to meet the needs for current formulations. What was once an important part of pesticide regulation has under the EPA been gradually allowed to fall into relative insignificance. To my knowledge, most hospitals are not equipped nor inclined to evaluate disinfectants, unless they are a part of a large medical center with research facilities and make a special project out of disinfectant testing.

Historically, many hospitals depend on the fact that the products they are using have EPA registration numbers and are therefore placing their faith in Federal approval. It has been suggested that this function be relegated to individual States. Most States have not shown any interest in testing disinfectants and are unlikely to assume additional responsibilities of this kind unless accompanied by liberal amounts of government funds. It seems more efficient and logical to have one main center to perform testing and provide whatever technical support States currently doing testing would need. Like most public health issues, this responsibility rests squarely on the Federal Government.

In closing, I would like to reiterate that in my experience, disinfectants currently available to the public do not work as they are supposed to. We have encountered a substantial number of failures, especially against certain pathogenic organisms, such as Pseudomonas aeruginosa, an organism of critical importance in burn and surgical infections and patients whose normal resistance has been compromised by undergoing various therapies. It is difficult, if not impossible, to directly correlate the rate of hospital-acquired nosocomial infections with inefficacious products.

The November 24, 1978, issue of the Journal of American Medical Association noted that patients with hospital-acquired bacteriemias has a hospital stay that was 14 days longer than the average. How much of this could be attributed to ineffective products is difficult to tell.

The prevention of hospital infections is vastly more difficult than documenting the prevalence but the potential is unquestionably there. We are constantly being informed about newly recognized diseases such as AIDS. We cannot afford to remain complacent and allow these diseases to run rampant before instituting preventive measures. And I thank you and I would invite questions from members of the committee.

Senator SARBANES. Thank you very much, Mr. Shaffer. Ms. Rhodes.

STATEMENT OF MARTHA E. RHODES, PH.D., ASSISTANT COMMISSIONER, FLORIDA STATE DEPARTMENT OF AGRICULTURE AND CONSUMER SERVICES

Ms. RHODES. Thank you, Mr. Chairman, Congressman Scheuer. My name is Martha Rhodes and I'm currently Assistant Commissioner of the Florida Department of Agriculture and Consumer Services. I speak to you today as a person that has been involved in the testing of disinfectant products for the past 18 years. My academic training is in the science of microbiology.

The Florida Department of Agriculture and Consumer Services is a large State cabinet agency involved in regulation, enforcement and consumer services and affairs. Back in 1968, under Commissioner Conner, I established this program of disinfectant testing because at that time we had a large number of products that were being manufactured in our State that currently, in 1968, did not require registration by then USDA, who regulated pesticides at that time.

Once we began this testing, we saw the need to retain it as a consumer services item for citizens in the State because we found a large number of products that did not meet claims.

We expanded the testing to include all of those products going in interstate commerce, and also instituted a series of tests for our State department of general services, to ensure that our State would not buy for State institutions and hospitals any products that were ineffective.

I have, as part of the attachments to the prepared statement, various documents and charts indicating the statistical result of that 18 years of testing.

For every year since 1968, we have found roughly somewhere between 15 to 30 percent of the products we tested to fail one or more of their label claims, and to be ineffective.

I must admit to you that statistics can be somewhat misleading. The program we have in the State of Florida is not a random program. It is one in which we have focused on those products involved in health care institutions, those claiming use in surgical wards, intensive care wards, those in which advertisements clearly display uses of pictures of surgical wards and health care situations. We also focused very heavily on products that we found in the past to be ineffective, or companies with a higher than usual rate of failure.

We have had many reports from competing companies themselves, indicating to us that they have been testing some of the competing products and find them consistently to fail. We have shared back and forth with the other regulatory agencies in North Carolina, Virginia, and also the EPA lab in Beltsville, the results of our different testing programs and we have verified and validated each other's results.

I am very pleased with the cooperation we have had from EPA in the last few years, in that they have allowed the Beltsville laboratory to at least verify and validate some of the ineffective testing we have been doing in the State of Florida. So we applaud those cooperative efforts. We appreciate them very much and appreciate the efforts of many of those in industry to work with us to try to bring the products we found to be ineffective back into compliance.

Over the last 18 years we have tested over 3,300 samples of disinfectants. As I said earlier, I would have to say the average is about 20 to 25 percent of the products that are tested failed at least one or more claims. Generally they fail the claims against the organisms that are more difficult to kill, such as Pseudomonas, or the fungicidal claim. But this needs to change.

There is no mechanism, however, to estimate the total health impact or total cost of our nation's total health care for hospital disinfectants. However, we support and applaud the efforts of this committee to support reinstituting a program of Federal testing, and it has been a long-held view of our State to support this and we will continue to do so in any way possible.

The front page of our Tallahassee paper just this past week indicated that health care costs in this nation had escalated to $425 billion. Dr. Frank Engler in addressing the CMSA in 1982, gave an estimate that 2 to 5 percent of our total health care costs were specifically tied into the cost of these health conveyor disinfectants and health care products.

Representative **Scheuer**. Excuse me, what was his name?

Ms. **Rhodes**. Dr. Frank Engler.

Representative **Scheuer**. What percent?

Ms. **Rhodes**. Two to five percent. So if you were to calculate against the estimate of $425 billion, this is an astronomical cost just for this group of products.

Also, an additional recent report released by the Centers for Disease Control in Atlanta quotes the most recent stats on nosocomial diseases and indicated two different studies which would say that 2 to 5 percent of all patients in hospitals would succumb to some type of nosocomial infection.

I'll be the first to admit that it's difficult if not impossible to specifically document a body count or the number of cases of nosocomial infection that result from the application of infected product. However, an examination of advertisements of the products themselves would indicate that they are being advertised for use and for effectiveness in surgical wards, intensive care wards, and those critical health care situations.

Health care is a critical item for our nation, in terms of personal loss of well-being, of productiveness, of economic drain on the Nation and inability to curtail astronomical escalation. I feel we could ill afford to have a major class of products used in health care that do not meet product claims and that are not examined for their effectiveness by the Federal agency responsible for their registration and placement in the marketplace.

Our testing in Florida currently is on products, of course, whose registration is with the Environmental Protection Agency. And this registration has been on the basis of negative data filed with the EPA for registration, and this data has been performed as a result of the application of the AOAC use-dilution test, as well as other procedures.

I would indicate to you that for our test results in Florida, if we have an ineffective product, the statistics I quoted to you are for tests that have been verified by other States and by the EPA lab.

When we define a product as ineffective, it's because of several things. It either does not meet a specific label claim for a particular organism—and this is primarily as a result of having living bacteria remaining after exposure to the disinfectant; second, we have received in the last few years several samples of product in which the disinfectant was received with living bacteria growing in the disinfectant. One particular incidence had 140,000 Pseudomonas cepacia growing in the concentrated disinfectant received. This is an organism that's involved in many cases of nosocomial infection. Repeated sampling of the product verified that this contamination was present.

We had another horror story with a Florida company who, in addition to making hospital disinfectants, was making septic tank additives. They mistakenly placed their hospital disinfectant in drums that were to contain the septic tank additive. Septic tank additivies are composed of cultures of bacteria. Needless to say the hospital disinfectant was very heavily contaminated with organisms too numerous to count.

In addition to being ineffective against label claims, and these isolated instances of receiving products with bacteria growing in them, we also find that sometimes the disinfectants do not contain the percent of active ingredient they should contain or, in the past we have had dry product that did not contain a net weight of product stated on their label. We greatly support the effort of this committee and of this hearing to support the reopening and active participation of the Federal Environmental Protection Agency in a program of regulation and enforcement of these health care products. Our nation can ill afford to have any products utilized in health care which do not meet the claims under which they are sold to the consuming public.

I am pleased that our agency has been involved in this program of consumer protection longer than any other State in the Nation. But I'm not proud that within these United States there are currently only four States that have the broad testing program. We, within Florida, do not care to have a responsibility of the testing and the production of data for the rest of the country, for this is an improbable burden and it's one which we cannot appropriately bear with the staff and resources currently available to us. We don't have the jurisdiction outside the State of Florida to pursue needed enforcement when we do find ineffective products.

The Federal Government needs a regulatory program to properly determine compliance with label claims for registered pesticides, to at least validate some registration data being submitted to them and to verify regulatory and enforcement activities of those States and institutions choosing to engage in proper enforcement of disinfectant claims.

I have provided various statements to you. I will not go into each and everyone of those.

Senator SARBANES. They will all be included in the record.

Ms. RHODES. But I would like to make these concluding observations. Since the lack of budgetary support for EPA to continue this program, and their choice not to have this enforcement program, we basically have no regulation of a critical class of health care products with the exception of an examination of the written data submitted by the companies for registration.

Now, the data being utilized to register and to sell these products is being based on test procedures which the industry is quite willing to accept for registration, but is quite unwilling to have any regulatory agency apply them for enforcement once their products are on the market.

Efficacy data, as a general rule, for infection control professionals, is most often received from the company salesmen.

Regrettably, we, within Florida, have found that some hospitals currently refuse to allow State/EPA-designated inspectors to sample disinfectant products being used within their surgical and intensive care wards. One reason that they cite is fear of liability if the agents are found to not be in compliance.

The policy of relying upon industry in the private sector for such critical health care decisions I feel is an improper and invalid one, just as relying upon States for this information.

Hospitals also can ill afford the money, the budget, nor have the type of facilities necessary for this type of testing.

In conclusion, I would offer the following comments: There is no way to estimate the magnitude of the problem that faces us with ineffective disinfectants. Yes, we do have problems with test methodology, and I think you have heard presented to you today some comments related to that information. We have supported, for many years, the changing and the refinement of those tests. However, we at the State level would continue to pursue an active enforcement program until such time as those tests are changed and those tests are appropriately validated.

We have had numerous visitors within our State program. We welcome that. We welcome the challenge of any of our regulatory programs for review. But the point that can be made here is that, among the regulatory laboratories and those that have strict quality assurance programs, the ability to confirm test results on ineffective products has always been shown. This confirmatory process is particularly needed at the Federal level, since, as I mentioned earlier, States have limited jurisdictional bounds.

Additionally, it would follow that if the method has variability, that will be indicated to you, that this variability should be reflected in product—registration data should be reflected in product data submitted to EPA. In fact, most all registration data show minimal variation and generally 100 percent effectiveness. Does this mean selective data has been submitted for registration?

There's no way to estimate the magnitude of this problem. I couldn't agree more fully with those who dispute the fact that it is impossible to document whether any infections are caused by just such products. Even so, it is our conclusion that if a product makes a specific label claim to anyone involved in the health care situation, the product should live up to that claim. There is nothing more critical than the reliability of that label.

We respectfully call on you to support the reinstitution of such Federal regulatory testing and enforcement programs and also we would respectfully request that somewhere we should be able to require that health care institutions allow the products they are using to be tested for effectiveness. Thank you very much.

[The prepared statement of Ms. Rhodes, together with attachments, follows:]

PREPARED STATEMENT OF MARTHA E. RHODES

Mr. Chairman and Members of the Committee, my name is Martha Rhodes. I am currently Assistant Commissioner, Florida Department of Agriculture and Consumer Services. I speak to you today as a person who has been involved in the testing of disinfectants and antimicrobials for the past 18 years. My academic training is in the science of microbiology and I have attached a brief resume of qualifications for your written record.

The Florida Department of Agriculture and Consumer Services is a large state cabinet agency involved in regulation, enforcement and consumer services. I am pleased that I was able to establish a program for disinfectant testing at Commissioner Doyle Conner's direction when I joined the Department in 1968 as a microbiologist, later as a Bureau Chief, an administrative role over this testing program, and now as Assistant Commissioner of the Department since 1984. My comments to you today will be relative to our testing program within the state and our experiences over the past 18 years.

We applaud the efforts of this Committee to reinstitute testing of disinfectants at the federal level, and we reaffirm our long-held support of the need to reopen the EPA Beltsville laboratory.

We have tested over 3,300 samples of disinfectant products over an 18-year period since 1968. Consistently, 15 to 30% failed to meet one or more label claims and were judged ineffective. This must change. There is no mechanism to estimate the total health impact or the total cost to our nation's health care from ineffective hospital disinfectants; however, we support the complete necessity for federal standards and federal testing.

The front page of our Tallahassee paper on Tuesday, July 29, quoted an annual report released from Health & Human Services that indicated health care spending consumed $425 billion last year, the highest level in history and equivalent to 10.7% of the gross national product of the United States economy. Further quotations indicated that 53% of this amount went for hospital care and nursing home care.

An additional recent report (released by the Center for Disease Control in Atlanta quoting statistics of the National Nosocomial Infections Surveillance System, NNIS,) indicated that nosocomial or hospital acquired infections caused substantial morbidity and mortality, prolonged the hospital stay of affected patients, and increased direct patient care costs. Approximately 1% of all nosocomial infections cause death and 3% of these infections contribute to death. A rate of nosocomial infections during 1984 varied from 3 to 6% infections per 100 patients discharged in two studies. I was pleased to note in the summary that it indicated that antiomicrobial usage in NNIS hospitals was being assessed so that for selective nosocomial pathogens the relationship between usage and resistance can be evaluated.

Though companies would claim that even if their products are ineffective, they do not add to the rate of nosocomial infection; yet, their advertisements continue to prominently feature photographs of surgical wards, intensive care wards and critical health care situations.

Health care is a critical item for our nation in terms of personal losses of well being and productiveness, economic drain on the nation, and inability to curtail the astronomical escalation. We can ill afford to have a major class of products used in health care that do not meet product claims and that are not examined for their effectiveness by the federal agency responsible for their registration and placement in the marketplace.

Our testing is performed on products whose registration with the Environmental Protection Agency has been on the basis of negative data. The test results over the last five years have been verified repeatedly by other state regulatory enforcement laboratories, the EPA laboratory in Beltsville and several private laboratories contracted with our agency. Problems may exist with current tests; however, this method is that used by the industry to register their products with EPA and to place them on the market. Until such test methodology can be changed and until the registration of those products on the market is based on data other than current test methodology, the State of Florida will continue to pursue an active regulatory enforcement program to insure that antimicrobial pesticides do properly meet the label claims that they have made to the consuming public who is relying upon them in health care institutions, surgical wards and nursing homes.

I will admit to you that our sampling program is not a random program so statistics on ineffective products may be misleading. We have focused on those products used in hospital or health care situations for these are the most critical. For hospital products including both quaternary ammonium compounds and phenolic compounds, the ineffective rate encountered has consistently been approximately 20%.

When we define a product as ineffective within our regulatory and enforcement program, it is for one of several reasons. Primarily, it is due to viable or living bacteria being present in multiple tubes after exposure to the disinfectant that is supposed to kill them. We follow recommended guidelines of the Environmental Protection Agency.

Secondly, it has sometimes been due to living bacteria present in the disinfectants themselves. We also have found multiple lots of dry products that did not even contain the net weight of material claimed on labels. We have found products being sold in interstate commerce and on the Florida market that were not registered whatsoever with EPA or the state.

We greatly support the effort of this Committee and of this hearing to support the reopening and the active participation of the federal Environmental Protection Agency in a program of regulation and enforcement of these health care products. Our nation can ill afford any products utilized in health care which do not meet the claims under which they are sold to the consuming public. Products must effectively comply with the label statement under which they are sold.

I am pleased that our agency has been involved in the consumer protection program of antimicrobial pesticide enforcement longer than any other state. I am not proud, however, that within these United States there are currently only four states with broad testing programs. We, within Florida, do not care to have the responsibility of the testing and the production of data for the rest of the country for this is an improper burden and one which we cannot appropriately bear with the staff and funding currently available to us. We do not have jurisdiction outside of Florida to pursue needed enforcement. The federal government needs a regulatory program to properly determine compliance with label claims for registered pesticides, to at least validate some registration data being submitted to them and to verify regulatory and enforcement activities of those states and institutions chosing to engage in proper enforcement of disinfectant claims.

In 1982, we provided the letters before the closing of the EPA lab and have communicated every year thereafter, supporting the retention of EPA's enforcement program. I have worked with the Association of Food and Drug Officials, the Association of Official Analytical Chemists, we have provided resolutions to the Southern Association of State Departments of Agriculture and the National Association of State Departments of Agriculture, and resolutions have come from all of these groups supporting the need for federal action. The American Society for Microbiology has also supported such action. I was active until 1984 with a Task Force formed at our suggestion by the Association of Official Analytical Chemists to examine problems with the testing methods and our Department remains an active participant in that Task Force work.

May I offer these observations:

1. We basically have no regulation of a critical class of health care products with the exception of an examination of written data submitted by a company for registration.

2. The data being utilized to register and to sell these products is being based on test procedures which the industry is quite willing to accept for registration but is quite unwilling to have any regulatory agency apply them for enforcement once their product is on the market.

3. Efficacy data relied upon by infection control professionals is most often received from company salesmen.

4. Only four of fifty states currently have broad analytical enforcement programs.

5. Hospitals currently refuse to allow state/EPA designated inspectors to sample disinfectant products being used within their surgical and intensive care wards. One reason cited is fear of liability if the agents are found to be not in compliance.

6. The State of Florida has had numerous companies to come to us on a confidential basis to indicate to us their support of our continued enforcement and testing program since it supported those companies with responsible quality control programs.

7. The policy of relying upon industry and the private sector for such critical health care decisions is an improper and invalid one.

8. Testing in the past four years has been routinely verified between the three state labs, EPA, and additional private laboratories.

9. Hospitals cannot perform this type of testing routinely for themselves.

10. Ineffective products have been found by (a) selected sampling of those products claimed to be for use in hospital situations, (b) resampling of companies which have had previous problems relative to other products, (c) sampling of products found to be ineffective by previous EPA, North Carolina or Virginia records, (d) indications by competing companies, and (e) sampling by private laboratories.

Commissioner Conner initially began our regulatory testing program in Florida because in 1968, disinfectant products not going across state lines were not required to be registered by USDA who then regulated such products. Our program is three-fold: The Florida Department of Agriculture and Consumer Services under Commissioner Doyle Conner has been designated as the lead agency within the State of Florida in the matter of pesticide regulation and enforcement and as such, we have a broad state enforcement program on pesticides from inspection to testing for formulation, for pesticide residues in food, and for efficacy of antimicrobial claims. In addition to this state enforcement inspection and sampling, we have a longstanding grant from the Environmental Protection Agency. In 1959 we began a disinfectant testing program for our state Department of General Services to insure that those disinfectant products being purchased for widespread usage in state institutions had to meet all label claims before products would be purchased.

For the past two fiscal years, we have analyzed roughly 250 samples per year, of which 23% each year have been found to be ineffective. In 1984-85, we analyzed 206 quaternary ammonium compounds, 15% of which were ineffective and 58 phenolic products, 19% of which were ineffective. This past fiscal year, of the 200 quaternary ammonium compounds samples, 14% were ineffective and of the 44 phenolic samples, 38% were ineffective. Again, our specific statistics cannot be viewed as totally representative of the market since they select those products which have the most stringent claims or previous poor record.

The problems are not ineffective problems alone. In 1983, two different products were received with large numbers of microorganisms growing within the products. One happened to be a lot of disinfectant manufactured in the

State of Florida. The company also produced a septic tank additive which was composed of high numbers of living bacteria. Inadvertently, the hospital disinfectant was placed into the drums previously containing the septic tank additive and the samples were received by our laboratory after having been sampled in a hospital situation. The sample contained too high a number of bacteria to estimate. Additionally that year, a sample of an EPA registered disinfectant in interstate commerce manufactured in a northeastern state was received containing 140,000 living cells of Pseudomonas cepacia. This organism had been found in many nosocomial infections and many environmental situations. Of the approximately 27,000 nosocomial infections reported to CDC, the most frequest pathogens were Escherichia coli, Pseudomonas aeruginosa enterococci, and Staphylococus aureus. The product was immediately resampled and the second sample from this container was found contaminated with not only Pseudomonas cepacia but additional viable bacteria. Information was referred on to the Environmental Protection Agency for their enforcement since the company was outside of the state.

We have attached certain items from our files as well as a chronological listing of certain pertinent events. These are for your review.

1968 USDA severely criticized by GAO for failing to actively monitor the efficacy of disinfectants.

1970-71 Community hospital in Florida has epidemic of 54 cases of nosocomial *Pseudomonos cepacis* infection. Epidemiological investigation strongly suggested that all but three of the affected patients acquired an infection at the time of cystoscopy or bronchoscopy. Other reports of contaminated quaternary ammonium compounds also reported within this 1974 report of the Center for Disease Control *National Nosocomial Infections Study*.

1974 EPA critized by GAO for not conducting agressive disinfectant testing program.

1980 Nine patients after open-heart surgery suffer serious infection from *Serratia marcescens* growing in the disinfectant utilized by the hospital. Article out of December 1980 *Lancet* attached. Attachments presented previously by Senator Gore indicate a product received in EPA labs that same year also contaminated with living *Serratia marcescens* bacteria.

1982 Newspaper reports Florida enforcement program bring dispute between government agency and industry over the effectiveness of the testing.

1982 Hospital infection control report on effectiveness of disinfectants.

1983 Florida presents results of disinfectant enforcement program to the Chemical Specialties Manufacturers Association Conference in Chicago and called for EPA to permit Beltsville laboratory to reopen for verification testing in instances involving conflicting results. Florida also called for cooperative effort to resolve methodology problems and cites only alternative is to notify those companies with repeated confirmed violations of our intent to suspend or deny registration.

1983 Report to the Environmental Protection Agency relative to receipt of contaminated lot of disinfectant sold in interstate commerce.

1983 Anonymous letter received from concerned EPA employees deploring EPA's decision to eliminate disinfectant testing and citing Supreme Court decision of March 5, 1983, requiring the screening of copycat drugs for safety and effectiveness by the Food and Drug Administration.

1983 EPA reports a failure rate of up to 20% of all disinfectants tested.

1983 EPA meets with Florida and other states to review proposed additional testing.

1983-86 Florida, North Carolina, Virginia and the EPA lab in Beltsville share results of listings of ineffective products and work cooperatively to confirm analytical results of each laboratory.

1986 Report in Hospital Infection Control citing data is lacking of safe, effective disinfectants and antiseptics. Estimate by Dr. Frank Engley at CSMA's 1982 annual meeting was that in the health care field at that time in 1982, $60-70 million was being spent on disinfectants, with $50 million in hand soaps, $29 million in floor care, and $20 million in odor control,. Estimation of antimicrobial products was 2-5% of health care dollars. We currently find ourselves in a deplorable situation within the United States. If Dr. Engley's estimates still hold true, our country is spending somewhere between $8-10 billion for products which do not live up to their claims of effective killing and control of pathogenic microorganisms which can be found in hospital and health care situations.

In closing, Ladies and Gentlemen, you may hear presented to you today various pieces of information related to the inadequacy of the testing procedure. There are very reputable and qualified professionals in EPA, in the industry and in the state regulatory programs. However, we at the state level have had our abilities and our laboratory results challenged because of such testing differences as using distilled or demineralized water or the choice of one type of serum over another to test efficacy under organic soil load. In relation to challenges, we have had numerous visitors within our laboratory who have conducted side-by-side testing. We have split samples with other states to confirm our results. The point that can be made here is that among regulatory laboratories and those who have strict quality assurance programs the ability to confirm test results has always been shown. This confirmatory process is particularly needed at the federal level since states have limited jurisdictional bounds. Additionally it would follow that if the method has variability that will be indicated to you, this variability would be reflected in the product registration data submitted to EPA. In fact, most all registration data shows minimal variation and generally 100% effectiveness. Does this mean that selective or prejudiced data has been submitted for registration?

Should not hospitals be required to demonstrate they are using effective products before licensure is granted?

Ladies and Gentlemen, there is no way to estimate the magnitude of the problem that faces us with ineffective disinfectants. I could not agree more fully with those who dispute the fact that it is impossible to document whether any infections are caused by such products. Even so, it is still our conclusion that if products make specific label claims they must indeed meet those label statements. We place a tremendous faith in the reliability of the printed word on consumer products. There is nothing more critical than the reliability of our faith in the printed claim of these products involved in health care.

We respectfully call on you to (1) support reinstitution of a federal regulatory testing program and (2) require hospitals and health care institutions to allow sampling of products they are using and require them to utilize effective products.

Thank you for allowing me the opportunity to offer these comments. If you or any of your staff have any questions we may answer or clarify, please contact us.

ATTACHMENTS TO STATEMENT BY DR. MARTHA E. RHODES

August 7, 1986

1. Resume of Martha E. Rhodes, Ph.D.
2. Newspaper article from Tallahassee Democrat, July 29, 1986
3. National Nosocomial Infections Study
4. Newspaper article from St. Louis Post-Dispatch, December 27, 1980
5. Article from the Lancet, December 13, 1980
6. Newspaper articles (3) from various papers on effectiveness of disinfectant testing, December 1982.
7. Newspaper article on Hospital Infections' Cost Cited, 1982
8. Letter to EPA, February 18, 1983
9. Letter from EPA employees, March 23, 1983
10. Article on CDC study from Professional Education Publications
11. Article from Pesticide & Toxic Chemical News, August 3, 1983
12. Newspaper article on EPA's halting of disinfectant tests, March 3, 1963
13. Article from Pesticide & Toxic Chemical News, August 24, 1983
14. Hospital Infection Control, March 1983 issue
15. Article from Chemical Times & Trends, October 1983
16. Article from Chemical Times & Trends, October 1983
17. Nosocomial Infection Surveillance, 1984
18. American Clinical Products Review, August 1984
19. Letter to Department from EPA, December 4, 1985
20. Report from Hospital Infection Control, March 1986
21. Departmental reports on disinfectant analyses

MARTHA E. RHODES

DATE OF BIRTH: August 11, 1939

PLACE OF BIRTH: Oxford, Mississippi

PRESENT POSITION:

Chief, Bureau of Food Laboratory, Division of Chemistry
Florida Department of Agriculture and Consumer Services
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Tallahassee, Florida 32301

1972 to present

EDUCATION:

B.S. in Biology - Summa cum laude, 1960
North Georgia College
Dahlonega, Georgia

M.S. in Bacteriology, 1961
University of Georgia
Athens, Georgia
Thesis: The Effect of Some Cations on the Induction of Enzymes in Marine Bacteria

Ph.D. in Microbiology, 1965
Department of Microbiology
University of Georgia
Dissertation: Effects of Cations on Enzyme Induction and Substrate Transport in Marine Bacteria
Major Professor: Dr. W. J. Payne

Public Health Postdoctoral, 1965-67
Department of Microbiology
University of Georgia
Athens, Georgia

Various Short Courses in Nutrition, Food Safety, Seafood Sanitation, Low Acid Canned Foods

PROFESSIONAL ORGANIZATIONS:

Association of Food and Drug Officials (International Association of State, Federal and Territorial Food and Drug Officials)
Institute of Food Technologists - National
Florida Section, Institute of Food Technologists
American Society for Microbiology - International
Southeastern Branch, American Society for Microbiology
Association of Food and Drug Officials of the Southern States
Association of Official Analytical Chemists
Sigma Xi
International Association of Milk, Food and Environmental Sanitarians
Florida Association of Milk, Food and Environmental Sanitarians
American Association for the Advancement of Science
American Chemical Society, Food and Agricultural Chemistry Section
American Public Health Association

HONOR SOCIETIES AND AWARDS:

Phi Beta Kappa
Phi Kappa Phi
Sigma Xi (full member)
Who's Who in American Colleges and Universities, 1958-59, 1959-60
Nu Gamma Scholastic Honorary Society (President, 1959-60)
American History Award, 1960, North Georgia College
Siler Award, 1960
North Georgia College, Highest Scholastic Award
Phi Sigma Award for Excellence in Graduate Research, 1963
University of Georgia
President's Award - Junior Researcher Award -1964
Southeastern Branch, American Society for Microbiology
Alumni Foundation Fellowship - two years - University of Georgia
Grade A Team Award, 1978, to Dr. Martha E. Rhodes and Staff
in Recognition of Special Team Effort
Presented by FDACS, Division of Dairy Industry
P. R. Edwards Award - 1979
Southeastern Branch, American Society for Microbiology
Diamond Jubilee Award
Recognition of Outstanding Abilities and Competence in Administration and Enforcement of Food and Drug Law and the Leadership and Guidance Provided to Fellow Workers. Presented in 1984 in Commemoration of the 78th Anniversary of the Enactment of the Federal Pure Food and Drug Law by the Association of Food and Drug Officials and The Association of Food and Drug Officials of the Southern States

MAJOR WORKSHOPS ORGANIZED:

Food Mycology - Association of Official Analytical Chemists, Atlanta, Georgia, 1978
Food Toxicology - Association of Food and Drug Officials, New Orleans, Louisiana, 1982
Staphylococcal Enterotoxin in Foods
Food Adulteration Symposium - 1982 Association of Official Analytical Chemists
Detection of Juice Adulteration - Association of Food and Drug Officials, New Orleans, Louisiana, 1983
Disinfectant Efficacy Testing - Association of Official Analytical Chemists, Philadelphia, Pennsylvania, 1984

INVITED SPEAKER:

Institute of Food Technologists, Florida Section
Association of Food and Drug Officials
Association of Food and Drug Officials of the Southern States
Nutrition Education Seminars, Florida State University
ABC Research Corporation Technical Seminars
Florida Meat Packers Association
Florida Environmental Health Association
Florida Dietetic Association
Southeastern Poultry and Egg Association
Food and Drug Administration Training Courses
Chemical Specialties Manufacturers Association

OFFICES AND COMMITTEES:

Association of Food and Drug Officials

1983-84	President
1982-83	President-Elect
1981-82	Vice President
1979-81	Chairman, Science and Technology
1979-80	Chairman, Nominating Committee
1977-79	Vice Chairman, Education and Training Committee
1978-80	Program Committee

Association of Food and Drug Officials of the Southern States

1978-79	President
1977-78	Vice President
1978-80	Board of Directors, Executive Committee, Chairman, Technical Committee

U.S. Department of Agriculture, Microbiology Subcommittee of the Meat and Poultry Inspection Laboratory Committee, 1970-72

Association of Official Analytical Chemists

1984	Organizer - Symposium on Disinfectant Testing, Philadelphia
1983	Organizer - Detection of Juice Adulteration Workshop
1982	Organizer - Food Adulteration Symposium
1982	Food Toxicology Workshop
1978	Chairman, Food Mycology Workshop

State Participation Committee

American Society for Microbiology - National

1982	Local Arrangements Committee
1983-86	Branch Organization Committee

American Society for Microbiology - Southeastern Branch

1981-82	President
1980-81	President-Elect

Policy Chairman

Florida Association of Milk, Food and Environmental Sanitarians

1980-1981	Board of Directors

Florida Section of Institute of Food Technologists
Education Committee
Program Committee

National Conference on Food Protection

1983	8 member Steering Committee
1983	80 member Study Committee
1983-85	Co-Chairman, Continuing Conference Structure

Association of Officials Analytical Chemists

1982-84	Task Force on Disinfectant Methodology

AFDO/FDA Working Group on Bulk Food Merchandising, 1983

OTHER PROFESSIONAL EXPERIENCE:

Secretary and Laboratory Assistant in Zoology, Comparative Anatomy, Cat Anatomy, Bacteriology and Medical Technology - 1957-60, North Georgia College

Laboratory Assistant in General Bacteriology Courses - University of Georgia

Instructor, General Bacteriology 350 - University of Georgia

Research Associate, Microbiology Department - 1965-67, University of Georgia

Consultant, Microbiology - North Georgia College

Microbiologist/Chemist, Food Laboratory, Florida Department of Agriculture and Consumer Services, 1968-70

Assistant Chief, Food Laboratory, Florida Department of Agriculture and Consumer Services, 1970-72

Chief, Bureau of Food Laboratory, Florida Department of Agriculture and Consumer Services, 1972 to present

Related Experience: Presents 20-30 Presentations to Consumer and Professional Food Related Societies Per Year with 10-15 Television and Radio Programs Related to Food Topics Per Year.

CONSULTANT:

Food and Drug Relations
Food Microbiology
Antimicrobial Pesticides Testing
Food Labeling
Government Interactions

PUBLICATIONS:

BOOKS

Rhodes, Martha E. (Editor), Food Mycology, G. K. Hall and Company, Boston, Massachusetts, 1979

Rhodes, Martha E. (Editor), Detection of Juice Adulteration, Association of Food and Drug Officials, 1983-84 (in press).

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is "an overwhelming and growing body of evidence" that the binary weapons now under development – particularly the Bigeye bomb – may never be "capable of fulfilling their deterrent role."

Tallahassee Democrat 7/29

Health-care spending rises

WASHINGTON – Health-care spending consumed $425 billion last year, the highest level in history and equivalent to 10.7 percent of all goods and services produced by the U.S. economy, the government said Tuesday.

The annual report released by the Health and Human Services Department showed spending on health care remained on its historical upward track in 1985, but at a significantly slower pace than in past years.

The 10.7 percent of gross national product devoted to health care was the highest on record and compared with 10.3 percent in 1984 and only 5.9 percent in 1965.

But the rate of growth was the slowest in 20 years. Health expenditures in 1985 were up only 8.9 percent from 1984's $390.2 billion, the second year in a row the increase was below the double-digit levels of the previous two decades.

The $425-billion total health-care expenditures included medical research, construction and administration. The portion paid for personal health care was $371.4 billion in 1985.

Of that figure, 45 percent, or $167 billion, went for hospital care; 22 percent, or $83 billion, was spent on doctors; and 9 percent, or $35 billion, was spent on nursing-home care.

Economists who prepared the report said the slowdown was "attributable almost entirely to lower growth of prices" throughout the U.S. economy.

And they cautioned that two disquieting signs appear in the figures: The rise in medical prices still outpaced inflation for other goods and services, and early signs are that medical inflation began heating up again in late 1985.

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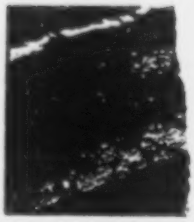

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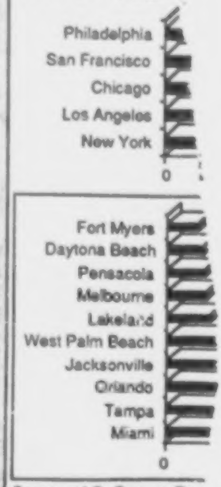

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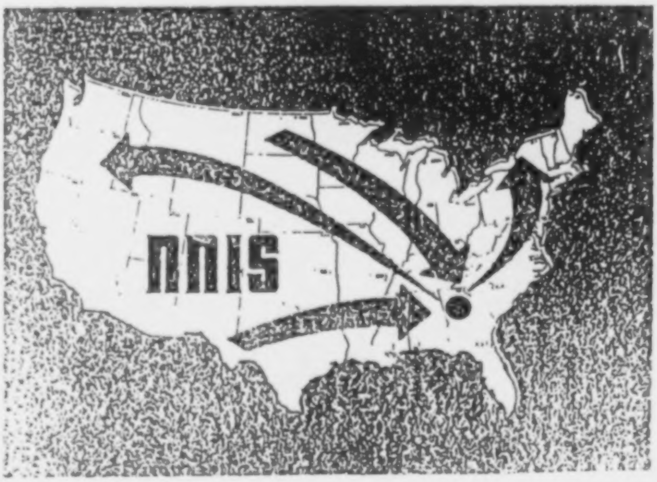
NATIONAL NOSOCOMIAL INFECTIONS STUDY



U. S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

METHODS OF PREVENTION AND CONTROL OF NOSOCOMIAL INFECTIONS

Disinfectant or Infectant: The Label Doesn't Always Say

Antiseptics (used to control organisms on skin and mucous membranes) and disinfectants (to kill pathogens on inanimate surfaces) do not necessarily sterilize surfaces to which they are applied under usual conditions of use in hospitals; rather, they are used to reduce surface contamination to a level considered unlikely to be hazardous. Their effectiveness depends, in part, upon the strength and activity of the agent, the duration of its contact with the contaminated surface, and the nature and extent of the contamination being treated. Unfortunately, antiseptics and disinfectants used in hospitals may not be effective in reducing contamination or may, on occasion, even themselves be contaminated.

Aqueous quaternary ammonium compounds (AQACs) appear to be especially prone to problems; for example, in a recent 10 month period, we investigated 4 separate outbreaks of disease associated with use of these agents. In 2 episodes, AQACs were used as disinfectants and were ineffective in preventing contamination of medical instruments; in the other 2 episodes, they were contaminated with viable organisms while in use as antiseptics. Each episode resulted in patient disease or suggested disease which led to administration of antimicrobial therapy.

Reports of Outbreaks:

Between January 1970 and August 1971, a community hospital in Florida had an epidemic of 54 cases of nosocomial *Pseudomonas cepacia* infection (1). The majority of the infections involved the urinary tract, but septicemia, surgical wound, and respiratory infections also occurred. Of patients from whom *P. cepacia* was isolated, 46% had evidence of clinical disease caused by the organism. Epidemiologic investigation strongly suggested that all but 3 of the affected patients acquired infection at the time of cystoscopy or bronchoscopy. Both cystoscopes and bronchoscopes were routinely disinfected in a freshly prepared 1:750 dilution of an aqueous benzalkonium chloride solution. There was no evidence that the disinfectant was contaminated, but it apparently did not eradicate contamination introduced at the time the endoscopic devices were treated. When glutaraldehyde was substituted for the quaternary ammonium disinfectant, the outbreak promptly ceased although other measures, introduced previously, had not effectively controlled the outbreak.

Between January 1971 and April 1972, 34 patients in a Georgia hospital were affected in a remarkably similar outbreak. There also, clinically important *P. cepacia* infections were significantly associated with prior cystoscopy. The epidemic organism was isolated from a basin used to disinfect cystoscopy instruments. In the hospital, cystoscopes were also disinfected with a 1:750 dilution of aqueous benzalkonium chloride prepared according to the manufacturer's instructions. When glutaraldehyde was introduced for disinfecting the instruments, the outbreak was brought under control.

In June 1972, CDC was notified by a Kentucky hospital that unusual pseudomonads were isolated repeatedly from blood of hospitalized patients. A resulting investigation by the hospital indicated that a commercially distributed quaternary ammonium antiseptic was intrinsically contaminated. The antiseptic was distributed in jars of 100 swabs, each swab containing approximately 1cc of a 1:500 dilution of aqueous benzethonium chloride.

Fifteen unopened jars were obtained by CDC from an Atlanta distributor. On culture using appropriate neutralizing agents*, 13 of 15 jars were shown to be intrinsically contaminated. Eight different organisms were isolated from these jars (Table 1), and the swabs grew between 10^2 and 10^5 organisms per cc (Table 2).

TABLE 1

MICROORGANISMS ISOLATED FROM CONTAMINATED AQUEOUS BENZETHONIUM CHLORIDE

Pseudomonas cepacia
Moraxella osloensis
Non-fermenter Group IIIa
Unidentified Pseudomonas species
Flavobacterium species
Corynebacterium species
Bacillus species
Lactobacillus species

TABLE 2

INTRINSIC CONTAMINATION OF COMMERCIALLY SUPPLIED AQUEOUS BENZETHONIUM CHLORIDE

Jar #	Organisms Per Swab
1	1×10^2
2	1.2×10^4
3	1.4×10^4
4	2×10^4
5	2.5×10^4
6	9×10^4

The fourth episode also involved contaminated antiseptic solutions. Between April 1971 and March 1972, 51 patients in a Virginia hospital had apparent bacteremia with a pseudomonas species subsequently identified at CDC as *P. cepacia*. Of the 51 patients, 31 (61%) had a blood culture positive for the organism drawn within 24 hours after admission; thus, nosocomial acquisition seemed quite unlikely. Furthermore, fewer than 1/4 of affected patients had exposure to any common factor other than venipuncture prior to isolation of the organism. Finally, only 3 of 38 patients whose charts were intensively reviewed had clinical or laboratory evidence of true bacteremia. Thus, artifact was strongly suspected. Cultures of a 1:750 dilution of aqueous benzalkonium chloride used at the time of blood culturing for venipuncture antisepsis showed contamination with *P. cepacia, Enterobacter cloacae, Enterobacter agglomerans* and *Serratia marcescens*. In retrospect, the hospital had experienced a high frequency of enterobacter isolates also, but had not recognized this as unusual. Substituting phor antisepsis prior to venipuncture resulted in control of this eudobacteremia epidemic.

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* 0.7% soy lecithin and 0.5% polysorbate 80 in Brain-Heart Infusion Broth enriched with 0.5% beef extract.

Discussion:

Over 15 years ago, editorials in The Lancet and The British Medical Journal (2,3) warned of potential problems associated with the use of aqueous quaternary ammonium compounds (AQACs) for, by that time, outbreaks of human disease resulting from inactivation or contamination of these agents had been reported (4). Nonetheless, AQACs continued to be used, and descriptions of associated problems continued to be reported (5-10). One of the outbreaks involved intrinsic *P. cepacia* contamination of aqueous benzalkonium chloride included, for meatal cleansing, with a commercially distributed urinary catheter kit (11). In 1970, an editorial again cautioned against their use (12). But the use of these products in hospitals continues, as do outbreaks of human disease (13). Thus, the 4 episodes described above are not unique. The episodes do, however, again raise 3 questions: why are these agents apparently ineffective; why do they continue to be used; and what alternatives are available to hospitals that wish to avoid potential problems associated with the AQACs?

Why are AQACs sometimes ineffective? At least 2 mechanisms have been proposed. First, as with any antimicrobial, genetic or acquired resistance may be present. In this regard, AQACs appear especially ineffective against pseudomonas species, particularly *P. cepacia*. In fact, a cetrimide-based culture medium is used in our laboratories to isolate *P. cepacia* selectively. Second, AQACs appear especially prone to inactivation by organic material. Cork used in stoppers (14,15) or gauze (7) have been documented to inactivate these products. In addition, many commercial products contain metabolic substrates for microbial growth (16).

With the extensive evidence that AQACs can be ineffective, why are they still used? Any answer must be quite speculative. Cost may be 1 factor since some of these agents are substantially cheaper than other antiseptics and disinfectants currently marketed. AQACs are also relatively nontoxic and allergic reactions are apparently rare although they have been reported (17). Furthermore, AQACs neither cloud lensed instruments nor do they etch metal ones. Finally, they may be used--and misused--because hospital personnel remain unfamiliar with their potential risks; in all probability, these personnel tacitly assume that any agent, marketed and available to the hospital as an antiseptic or disinfectant, *must* be effective.

What alternatives are available to hospitals in selecting antiseptics and disinfectants? No ideal antiseptic is currently available since all have a potentially limited antimicrobial spectrum as well as various problems with irritation, hypersensitization, or personnel acceptance. Nonetheless, there are alternative agents equal to or surpassing AQACs in safety and effectiveness for antiseptic and disinfectant purposes for which AQACs have been widely used in the past.

For example, many agents appear preferable to the AQACs for skin and mucous membrane antisepsis. Tincture of iodine or 1-3% iodine in 70% alcohol have broad antimicrobial spectra and little likelihood of being contaminated; however, some patients are allergic to iodine and most clinicians are hesitant to use these agents on sensitive mucous membranes or denuded skin. Organic-bound iodines--the iodophors--also have a broad antimicrobial spectrum and also appear to offer a relatively low risk of intrinsic contamination; they must be vigorously applied and must not be rinsed off since their effectiveness appears to result, in part, from slow release of inorganic iodine. Side effects appear to occur rarely, and these agents have been used on mucous membranes. For patients sensitive to iodine-containing compounds, a soap and water scrub followed by a 2-minute scrub with 70-90% isopropyl or ethyl alcohol offers effective antisepsis for most purposes. Hexachlorophene-containing agents can be contaminated with gram-negative bacteria (18,19) and may predispose to overgrowth with these organisms (20,21); however, hexachlorophene is still useful for antisepsis where activity against gram-positive cocci, such as staphylococci, is important such as for personnel handwashing in the newborn nursery.

Medical devices that enter tissues must be sterile; steam, hot air, or properly performed ethylene oxide sterilization is necessary before these items can be used. For supplies that cannot be sterilized by one of these more preferable methods (and many items such as inhalation therapy and anesthesia apparatus, intravenous catheters, and endoscopic devices can be so treated), either carefully performed pasteurization (22,23) or disinfection with gluteraldehyde is far more effective than use of AQACs.

For other types of surface sanitation, such as the environmental cleaning of floors, furniture, etc., vigorous physical cleaning with a freshly prepared solution and clean equipment is probably more important than the specific nature of the detergent-germicide used. We have not documented patient disease problems associated with use of AQACs for cleaning these surfaces, and, at this time, any of the Environmental Protection Agency registered detergent-germicides appear appropriate for these uses. As we have noted previously, we do not recommend disinfectant fogging of hospital areas (24), another purpose for which these agents have been used.

The quaternary ammonium compounds may have specific indications for which they are uniquely qualified. Cleansing of wounds inflicted by potentially rabid animals is one indication often noted, but most studies showing experimental effectiveness of the AQACs have used far higher concentrations of AQAC (at least 1% solution) than are normally used in hospitals and have found that the lower concentrations, such as those generally used in hospitals, have less efficacy (25). Furthermore, when tested, 50% alcohol was as effective as the concentrated AQAC (26). Iodophors have not been tested in these situations.

AQACs are also occasionally instilled into the conjuctival sac prior to ophthalmic surgery. None of the other antiseptics noted above is approved for this use. If a topical antiseptic for this site is judged necessary--some physicians do not use any agent--we believe that the antiseptic must be assured potent and sterile.

AQACs are also included in some prepackaged urinary catheter kits. Under these circumstances, the risk of intrinsic contamination is probably small, but even these unit-dose AQAC antiseptics can be contaminated (11). Accordingly, we think that other agents, such as the iodophors, would be preferable for these purposes.

Thus far, we have discussed the *aqueous* quaternary ammonium compounds. Tinctures of quaternary ammonium compound, where alcohol is added, are also available. These agents appear not to be as prone to problems of inactivity or contamination, probably because of the antimicrobial effect of the alcohol. In fact, it appears that it is the alcohol, not the quaternary ammonium component, that is primarily responsible for the antimicrobial effect of these agents (27,28).

We have not evaluated the effectiveness of all AQACs currently available, and we cannot generalize with certainty that the problems noted above would be encountered with all available agents. However, we are aware of no experimental data or theoretical rationale to suggest that any of the currently available aqueous quaternary ammonium compounds are free of these problems. Although each antimicrobial can be misused, other agents may also be intrinsically contaminated on occasion (29), and even recommended agents may be ineffective under some conditions of use (30), we believe that the balance of evidence, now available, suggests that the hazards of use and misuse of AQACs outweigh their potential benefits. Thus, the Hospital Infections Section believes that hospitals choosing to use these agents as antiseptics or to disinfect medical supplies should do so with great caution and should recognize their obligation to assure that these agents are used safely.

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102, No. 356

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SATURDAY, DECEMBER 27, 1980

Heart-Machine Bacteria Infect 9 Patients In Miami Hospital

MIAMI (UPI) — Nine patients who underwent open-heart surgery in a Miami hospital contracted a serious infection from bacteria that had lodged in the heart-lung machine and was immune to the disinfectant sprayed in the operating room, investigators report.

Dr. N. Joel Ehrenkranz, a physician specializing in infectious disease, said that investigators found 11 patients who were exposed to the serratia marcesacens bacteria while undergoing surgery. Nine became infected and "four had very serious infections," he said, that required prolonged hospitalization and, in one case, a second operation.

The incident and investigation by a four-member team from the South Florida Consortium for Infection Control is described in the current issue of the British medical journal Lancet.

"These organisms can be a particular problem if they get into the heart pump, and that's where they got," Ehrenkranz said. "We were very fortunate, very lucky. We were able to identify the contaminating source very quickly and get it out of the heart pump almost immediately."

He said all nine victims recovered. But three of the four had to spend at least two additional months in the hospital and the fourth had to undergo a second operation for replacement of an infected heart valve.

"Some microbes can develop immunity to disinfectant. Just because the label says the product (disinfectant) has been approved ... doesn't mean the problem won't arise," he said.

Ehrenkranz said that the hospital involved, which he declined to identify, is considered an "excellent hospital and has had no trouble since then."

Ehrenkranz said hospital employees sprayed the floor with disinfectant immediately before each surgery was performed.

Although the employees were under orders to prepare a new supply of disinfectant daily and sterilize the container before it was filled, they kept the left-overs and topped off the bottles, which allowed bacteria to grow in them and become immune.

The Lancet article reported that the germs were transmitted from the operating room floor to the heart-lung machine by the hands of a technician who touched the floor while preparing the mechanism. During surgery, a small amount of disinfectant entered the machine through a joint in the tubing and was pumped into the patient's blood.

Ehrenkranz said the disinfectant involved was an ammonium substance. He said other disinfectants, such as phenolics and polyvidone iodine, may be used as alternatives, "but nothing is totally without the possibility of failure."

Joan Knock of the University of Reading who handled all the data, prepared the computer programmes, and analysed the data.

Requests for reprints should be addressed to W. E., West Berkshire Health District, 3 Craven Road, Reading, Berks RG1 5LP.

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Hospital Practice

ANTIBIOTIC-SENSITIVE *SERRATIA MARCESCENS* INFECTIONS COMPLICATING CARDIOPULMONARY OPERATIONS: CONTAMINATED DISINFECTANT AS A RESERVOIR

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Summary A cluster of *Serratia marcescens* infections complicating cardiopulmonary bypass operations was traced to contaminated quaternary ammonium disinfectant. Failure of hospital personnel to clean the disinfectant spray bottles before refilling them had enabled the organisms to survive and contaminate the environment, including the extracorporeal circulator. The organisms grew in two of four formulations of quaternary ammonium disinfectant. *Serratia* sensitivity to ampicillin and tetracycline was an epidemiological marker of a common-source outbreak.

INTRODUCTION

Serratia marcescens has a wide distribution in nature and thrives in moisture. It is not generally part of healthy human microbial flora,[1] although the organism has been recovered from hands of hospital personnel,[2-6] which have become transiently colonised after contact with infected patients' secretions or contaminated solutions. Quaternary ammonium disinfectants are widely used in hospitals to reduce the number of such microorganisms in the environment and prevent cross-infection. Unfortunately, contamination with some *Pseudomonas aeruginosa* or *Ps. cepacia* strains which are inherently capable of growth in the disinfectant can lead to outbreaks of infection.[7,8] This report describes a cluster of nosocomial infections due to *S. marcescens* distributed in a quaternary ammonium disinfectant. The infecting strain was unique in its ability to multiply in some but not all quaternary ammonium disinfectants and had a distinct marker of antibiotic sensitivity.

CASE CLUSTER AND DEMONSTRATION OF CIRCULATOR CONTAMINATION

In June and July, 1978, two patients at one hospital developed transient *Serratia* bacteremia after cardiac operation requiring cardiopulmonary bypass with extracorporeal circulation. In August, 1978, the infection-control nurse initiated surveillance cultures of the extracorporeal circulator during each of eleven operations. Immediately before connection of the patient for cardiopulmonary bypass the Ringer's lactate solution used for priming the circulator was withdrawn for culture, and during the operation the patient's blood in the circulator was similarly cultured. Circulator contamination with *Serratia* was demonstrated in nine operations—two for aortic-valve replacement, three for mitral-valve replacement, and four for coronary-artery bypass. In three instances, circulator cultures made both before and after connection of the patient yielded *Serratia*. Two of these patients subsequently developed *S. marcescens* sternal-wound infection. In six operations, only the culture made during patient use yielded *Serratia*. One of these patients later developed endocarditis and required replacement of an aortic valve for cure; *S. marcescens* was cultured from the infected valve. Another patient eventually manifested *S. marcescens* sternal-wound infection.

INVESTIGATION

Review of operating-room practices and procedures for these operations revealed no apparent departures from standard practice, except on occasion when the circulator pressure manometer was not removed and sterilised after use, although this generally was done. Preoperative and postoperative antibiotic prophylaxis included cephalothin and gentamicin treatment. After each operation all circulator tubing was discarded. Fresh sterile tubing was connected immediately prior to operation.

More than 300 surveillance cultures of equipment, medications, disinfectants, room and equipment surfaces, air, fluids, and hands of operating-room personnel were made. Hands of one of two circulator technicians, the sink drain in a utility room, the ice chest used for intraoperative storage of chilled intravenous fluids, and three of four bottles of A33 disinfectant solutions in a spray bottle yielded *S. marcescens*. Intravenous fluids and ice sampled before storage in the ice chest, fluids used for the circulator, and the dry disinfectant yielded no *Serratia*.

A33 disinfectant had been in hospital use for six years and was sprayed preoperatively in the cardiac operating room as an environmental disinfectant. It was applied to the floor adjacent to the extracorporeal circulator, an area the pump technician touched while connecting tubes for priming the circulator. The dry disinfectant was freshly prepared and diluted in tap-water according to manufacturer's directions. However, spray bottles were refilled when partially empty and were not regularly emptied and cleaned before refilling.

After recognition of contamination in September, A33 was withdrawn from use and environmental disinfection of the operating room with spray bottles was discontinued. Cultures from the hands of technicians and other personnel no longer yielded *Serratia*. The pressure manometer was now routinely disassembled and sterilised. Surveillance cultures from the extracorporeal circulator before and during connection of the patient in seven operations were now sterile. No further episode of *Serratia* bacteraemia was detected in a 24-month follow-up.

METHODS

Surveillance Cultures

Cultures were made from the hands of physicians and operating-room personnel at the end of an operation after removal of sterile gloves, by immersion and rinsing of the hands in 10 ml of nutrient broth in a sterile plastic bag. Hands of ungloved personnel were similarly cultured during an operation. Airborne bacteria in the operating room were sought by exposure of blood-agar plates during operation. Swabs of floor and other surfaces, air-conditioning filters, and ice were placed into thioglycolate broth for culture. Fluids were cultured by aseptic transfer of 5 ml into 50 ml broth.

Identification of Organisms

Isolates were identified with standard biochemical procedures.[9] Antimicrobial susceptibility tests were done by the disc-diffusion method based on the Bauer-Kirby procedure[10,11] and the broth-dilution method[12] using 'Sensititre' plates (Gibco Diagnostics). The isolates were serotyped at the Center for Disease Control, Atlanta, Georgia. .

Disinfectants

Four quaternary ammonium disinfectants were tested. A33 Dry (Airkem Laboratories) contained n-alkyl (60% C14, 30% C16, 5% C18, 5% C12) dimethylbenzyl ammonium chloride (5·8%) and n-alkyl (68% C12, 32% C14) dimethyl ethylbenzyl ammonium chloride (5·7%), the in-use dilution being 1:256; TBQ (Vestal Laboratories) contained N, N, bis 2-omegahydroxypoly (oxyethylene) ethyl alkylamine (12%) and n-alkyl (50% C14, 40% C12, 10% C16) dimethyl benzyl ammonium chloride (8%), the in-use dilution being 1:256; TOR (Huntington Laboratories) contained n-alkyl (60% C14, 30% C16, 5% C18, 5% C12) dimethyl benzyl ammonium chloride (1·6%) and n-alkyl (50% C12, 30% C14, 17% C16, 3% C18) dimethyl ethylbenzyl ammonium chloride (1·6%), the in-use dilution being 1:64; and HI-TOR (Huntington Laboratories) contained n-alkyl (60% C14, 30% C16, 65% C18, 5% C12) dimethyl benzyl ammonium chloride (6·75%) and n-alkyl (68% C12, 32% C14) dimethyl ethylbenzyl ammonium chloride (6·75%), the in-use dilution being 1:128. Solutions were prepared according to the manufacturer's instructions.

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5%

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Microbial Susceptibility to Disinfectants

Organisms for testing were prepared from isolated colonies on a 5% sheep-blood agar plate which was incubated overnight. Bacterial cells were washed twice with deionised water, and the suspension was diluted to the desired concentration; 0·05–0·1 ml was used as an inoculum for 5–10 ml of disinfectant. The mixture was maintained at room temperature and samples were taken periodically to determine microbial viability. A disinfectant-resistant population of cells was maintained by continuous exposure to A33 disinfectant. The number of viable cells which could be maintained in the disinfectant was approximately 10^7 organisms/ml.

Conjugation

R-plasmid transfer experiments were attempted with a disinfectant-resistant isolate and a disinfectant-sensitive isolate using a modification of the procedure of Suenderhaul et al.[13]

Sudan-black B Stain for Bacterial Fat

Increased intracellular fat, considered an indicator of lack of permeability to quaternary ammonium disinfectant,[14] was determined with the Sudan-black B stain method as described by Chaplin.[14] Cells maintained in the A33 disinfectant for 7 days were harvested by filtration using 0·25 μm pore size filters (Millipore Corporation) and resuspended in deionised water before staining. Cells containing fat are darkly stained.

Calcium Determinations

Calcium-ion concentration in the water used to prepare the disinfectants was determined by atomic absorption spectrophotometry.[15]

RESULTS

Eight *S. marcescens* isolates from infected patients and surveillance cultures were serotyped. In one a somatic antigen was identified. Others could not be serotyped with the available 01–020 antisera. Isolates from one disinfectant bottle, the ice chest, and two patients were motile. The motile isolates possessed flagella antigen H8. Antibiotic-susceptibility testing showed that isolates were resistant only to cephalothin (see table).

Eight *S. marcescens* isolates obtained during the outbreak repeatedly survived exposure to A33 but were regularly killed by TOR and TBQ. On occasion isolates survived exposure to HI-TOR. *S. marcescens*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, and *Ps. cepacia* strains recovered from patients in other hospitals were killed by all disinfectants tested.

A minimum inoculum of 10^7 organisms/ml was necessary for the *Serratia* isolate to survive in A33 disinfectant. When A33 disinfectant solution was inoculated to a density of approximately 6×10^8 organisms/ml using organisms from an overnight growth on 5% sheep-blood agar, the viable count dropped to 10^1/ml within an hour of exposure at room temperature (fig. 1); however, continued incubation resulted in microbial multiplication. After 4 days the colony count

SEROTYPE AND ANTIBIOTIC SUSCEPTIBILITY OF *SERRATIA MARCESCENS* ISOLATES FROM THE CASE CLUSTER

Source	Serotype*	Minimal inhibitory concentration (μg/ml)							
		AMP	CB	CF	AMK	GM	K	CH	TET
Blood—Patient A	0 undetermined: H8	1	<4	32	0·5	0·5	2	2	2
Wound—Patient B	0 1 : NM	2	<4	64	2	0·5	2	8	4
Circulator—Patient C	0 rough : H8	2	<4	64	1	0·5	2	8	4
Circulator—Patient D	0 undetermined: NM	2	<4	128	2	1	2	8	4
Technician—hands	0 undetermined: ISM	2	<4	64	2	0·5	2	4	4
Disinfectant	0 undetermined: H8	2	<4	128	2	1	2	4	4
Disinfectant	0 undetermined: NM	4	<4	128	4	1	4	8	8
Ice chest	0 undetermined: H8	2	<4	128	2	2	4	4	4

AMP = ampicillin, CB = carbenicillin, CF = cephalothin; AMK = amikacin, GM = gentamicin; K = kanamycin; CH = chloramphenicol, TET = tetracycline.
*0 refers to the somatic antigen; H the flagella antigen; NM = non-motile; ISM = insufficiently motile for testing.

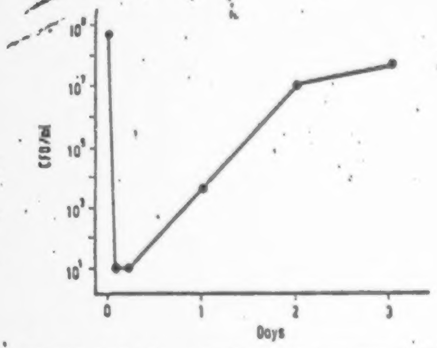

Fig. 1—Survival and growth of *Serratia marcescens* in A33 disinfectant at room temperature.

reached a plateau of 10^7/ml. The isolate when inoculated into tap-water, deionised water, or triple-distilled water at a concentration of 10^3/ml, grew to 10^5–10^6/ml within 4 days of incubation at room temperature.

Cells which grew in the disinfectant were harvested by centrifugation and re-exposed to fresh disinfectant at concentrations of 10^1 and 10^6/ml. These populations of cells had not decreased at 1 h but continued to multiply.

A33-disinfectant-resistant cells were tested against other quaternary ammonium solutions prepared in tap-water. Growth of A33-resistant cells occurred in A33 and III-TOR disinfectants but not in TBQ or TOR disinfectants (fig. 2).

Tap-water contained 2·3 mg calcium/dl. Adding ethylene-diamine-tetra-acetate (EDTA) to tap-water did not alter the susceptibility of the A33-resistant cells. A33 prepared with deionised water and inoculated with A33-disinfectant-resistant cells resulted in complete kill.

Conjugation experiments to test whether resistance was plasmid-mediated revealed no transconjugates.

A33-disinfectant resistant and susceptible cells examined with Sudan-black B stain for cell fat revealed no difference in staining intensity.

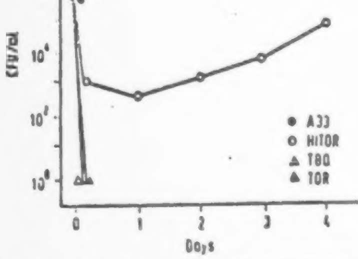

Fig. 2—Survival of A33-resistant *Serratia marcescens* in different quaternary ammonium disinfectants.

DISCUSSION

Persistence and growth of *Serratia* in the A33 disinfectant resulted from refilling of partially empty spray bottles. The contaminated disinfectant was sprayed on various operating-room surfaces, including the circulator, immediately before operation. The circulator is likely to have been contaminated from the technician's hands when he connected tubes for priming. On those occasions when the pressure monitor was not changed, it could have served as a secondary source of contamination. The danger of using quaternary ammonium compounds as disinfectants rather than cleansers is re-emphasised.[16] Hospital personnel cannot be relied upon to distinguish between disinfectants which can and cannot support microbial growth, although they should be expected not to top up solutions.

Serotyping of the *S. marcescens* isolates showed that only one isolate had an identifiable somatic antigen and several motile isolates had a common flagellar antigen. The somatic antigen in most of the isolates could not be determined. This suggests at least two populations of resistant cells. Interspecies transfer of genetic material carrying a resistance marker was not demonstrated.

The similarity in composition of the dimethyl benzyl ammonium and dimethyl ethylbenzyl ammonium chains in A33 and III-TOR disinfectants which supported *Serratia* growth is noteworthy. In contrast, neither TOR, which possessed a more complex dimethyl ethyl benzyl ammonium chain, nor TBQ, a dimethyl benzyl ammonium disinfectant that also contained an ethyl alkylamine compound, permitted growth. Tap-water but not distilled water diminished A33 disinfectant activity against the outbreak strain of *Serratia*. Quaternary ammonium compounds alter bacterial-cell membranes, and their activity is generally enhanced by EDTA.[17] Resistant strains of *Serratia* are reported to have extra lipid. However, the resistant isolates in this outbreak were not rendered sensitive in tap-water by EDTA, nor was increased fat demonstrated.

Many *Serratia* found in soil and water outside the hospital are sensitive to antibiotics (other than penicillin G, cephalothin, and colistin), whereas those recovered in hospitals are generally resistant to ampicillin and tetracycline.[18,19] *Serratia* outbreaks attributed to cross-infection of patients are characterised by plasmid-mediated antibiotic-resistance patterns and are associated with considerable antibiotic usage.[1] In this common-source outbreak the isolates were susceptible to ampicillin and tetracycline. In five of ten common-source outbreaks mentioned by Farmer and others, similar antibiotic-sensitive *Serratia* were described.[19]

We thank the Airwick and Vestal Companies for supplies of disinfectant reagents and Vestal for financial support. We also thank Dr D. Brenner and Ms B. Davis, of the Center for Disease Control, for aid in serotyping of *Serratia*.

Requests for reprints should be addressed to N.J.E., 1295 N.W. 14th Street, Miami, Florida 33125, U.S.A.

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References continued overleaf

Many disinfectants found ineffective in state-run tests

ASSOCIATED PRESS 12/27/82 (9D)

More than two dozen germ killers used to disinfect and sanitize hospitals, nursing homes and schools don't kill all the germs they're supposed to, according to state tests.

"It could be a very significant problem," said Martha Rhodes of the Florida Department of Agriculture's laboratory in Tallahassee, because ineffective germ killers contribute to "a very great problem with hospital infections."

About 30 percent of the germicide product samples brought to the lab failed to live up to claims of effectiveness, the microbiolgist told *The Fort Lauderdale News and Sun-Sentinel*.

The extent of the health problem posed by ineffective germ killers isn't known, said Barry Davis of the federal Center for Disease Control in Atlanta.

"It's not the primary route of hospital infections," Davis said, and officials "don't know enough about it to make it a major concern. It's something that should be looked into."

The 26 germicides that failed the state test in the past year have generally been liquids or aerosol sprays used to clean walls and floors in hospitals and other institutions.

The tests have triggered a strong reaction from the disinfectant industry, which has questioned the validity of the state tests.

"We stand by our products," said Ralph Engel, president of the Chemical Specialities Manufacturers Association, a trade association that represents germicide producers. "We are concerned about quality and efficacy. We are investigating what we consider (Florida's) unusual results."

Harry Rohme, a spokesman for Airwick Industries of New Jersey, which voluntarily withdrew its products from the Florida markets after poor test results last year, said his company is confident of the effectiveness of its products.

Because of the dispute between germicide makers and Florida, the Association of Official Analytical Chemists is planning to review the germicide tests. The group sets testing procedures for many drugs and pesticides.

JAN 3 1983

Hike in Gas Tax OKd by Senate

(10A)

12/24/82

Filibuster is broken by 81-5 vote

From Herald Wire Services

WASHINGTON — Senators anxious to go home for the holidays on Thursday smashed a conservative filibuster, passed President Reagan's nickel-a-gallon gasoline-tax increase and then, at 1:13 p.m., adjourned the 97th Congress.

Final approval of the tax measure — which hikes the federal tax on a gallon of gasoline from four cents to nine cents a gallon -- came two hours after the filibuster led by Sen. Jesse Helms (R., N.C.) was broken on a 81-5 vote, 21 votes more than necessary.

Highlights of Lame—Duck Session

- Congress approved a nickel-a-gallon boost in gas taxes.
- Both houses passed a stopgap funding bill to keep federal agencies operating until Sept. 1, 1983.
- $988 million in production money for the MX missile was killed. However, a record $232 billion for defense spending was approved.
- Money for jobs programs was stymied.
- The House voted itself a $9,138 raise, increasing the annual salaries of its 435 members to $69,800.
- Parts of Reagan's Caribbean Basin Initiative and the Radio Marti proposal for a station to beam broadcasts to Cuba were allowed to die.

he Miami Herald
londay, Dec. 27, 1982

State finds germ killers ineffective

[illegible] Press

More than two dozen germ killers used to isinfect and sanitize hospitals, nursing homes nd schools don't kill all the disease germs hey're supposed to, according to state tests.

"It could be a very significant problem," said lartha Rhodes of the Florida Department of Agiculture's laboratory in Tallahassee, because inffective germ killers contribute to "a very great roblem with hospital infections."

About 30 per cent of the germicide product amples brought to the Tallahassee lab fail to ve up to claims of effectiveness, the microbiolist said.

The extent of the health problem posed by ineffective germ killers isn't known, said Barry Davis of the federal Centers for Disease Control in Atlanta.

"It's not the primary route of hospital infections," Davis said, and officials "don't know enough about it to make it a major concern. It's something that should be looked into."

The 26 germicides that failed the Florida state test in the past year have generally been liquids or aerosol sprays used to clean walls and floors in hospitals and other institutions.

The state tests have triggered a strong reaction from the disinfectant industry, which has questioned the validity of the Florida tests.

"We stand' by our products," said Ralph Engel, president of the Chemical Specialties Manufacturers Association, a trade association that represents germicide producers. "We are concerned about quality and efficacy. We are investigating what we consider (Florida's) unusual results."

Harry Rohme, a spokesman for Airwick Industries of New Jersey, which voluntarily withdrew its products from the Florida markets after poor test results last year, said his company is confident of the effectiveness of its products.

Mugged man spent Christmas lost in coma

TAMPA — (AP) — Michael Muccino, who noved from Pennsylvania to Florida when an rie, Pa., toy factory closed, spent his first hristmas in Florida in a coma on a hospital bed.

"What's Christmas this year," his father, Saino Muccino, 71, asked, turning his palms upward to accent the question.

The younger Muccino has been in a coma ince Dec. 9, when two men used a hammer to hatter his skull and mugged him, authorities said. He has not regained consciousness since undergoing emergency brain surgery that night at Tampa General Hospital.

"Prayer is the only thing that keeps us going," said Michael's mother, Mary. His parents flew from Pennsylvania to Tampa to be near their son, who was listed in poor condition Sunday.

Muccino, 29, moved to Tampa three months ago and found a job as a $4.05-an-hour pot washer at Memorial Hospital. It brightened his Thanksgiving, he told his parents in a letter.

"I took the lab test [for the job] the day before Thanksgiving and was officially hired so I had a lot to be thankful for," he wrote. "I was a Thanksgiving I'll never forget. I just hope they are satisfied with my work and I can keep my job."

Muccino was mugged two weeks later as he walked along a street. His attackers have not been found.

Family hol
for sailor i

SATELLITE BEACH — (A
— A computer technician wh
set sail for England in a nine-fo
sailboat is five days overdue, b
his mother says she's certain he
safe

Wayne Dickinson, 33, beg
the 3,000-mile trans-Atlant
journey nearly two months a
in his 8-foot, 11-inch craft, Go
Tear. He was spotted Oct.
near Provincetown, Mass., b
hasn't been seen or heard fro
since.

"We feel his boat is unsink
ble. We're concerned, but w
feel he is all right," the adve
turer's mother, Peggy Dickinso
said Saturday.

A spokesman for the Briti
Coast Guard, however, wasn't
encouraging.

"At the most, he has a 50-
chance," said the spokesma
who asked not to be
"I wouldn't even giv

Tests: Not all germ killers adequate

12-26-82

By Alan Bavley
Medical Writer

More than two dozen germicidal cleaners — the disinfectants used to sanitize hospitals, nursing homes and schools — do not kill all the disease germs they are supposed to, state scientists say.

About 30 percent of the germicide product samples being brought to the state testing laboratory in Tallahassee are failing to live up to their claims of effectiveness, said Dr. Martha Rhodes, Florida Department of Agriculture microbiologist in charge of the tests.

"It could be a very significant problem," Dr. Rhodes said. Ineffective germicides might contribute to "a very great problem with hospital infections," she said.

In the past year, 26 germicidal products manufactured or distributed by 18 companies failed in state tests to live up to the claims made for them.

The germicides that failed state tests generally are liquids or aerosol sprays used to clean walls and floors in hospitals and other institutions. Some of the products also claim to be effective sanitizers of surgical instruments and hospital isolation wards.

The products are supposed to kill various forms of bacteria, viruses and fungus. Some make specific claims to get rid of the viruses that cause herpes and influenza and the bacteria that cause tuberculosis.

The products that failed include many made by the nation's largest manufacturers of germicides.

One of these manufacturers, Airwick Industries of Secaucus, N.J., has voluntarily withdrawn from the Florida market one of its products, A-33 Dry, following negative test results this year. Three other Airwick products also are on the failed list.

The Florida findings have triggered a strong reaction from the disinfectant industry, which has raised questions about the validity of Florida's testing procedures.

"We stand by our products," said Ralph Engel, president of the Chemical Specialties Manufacturers Association, a trade association representing many producers of germicides.

"We are concerned about quality and efficacy," Engel said. "We are investigating what we consider (Florida's) unusual results."

Harry Rohme, a spokesman for Airwick, said his company remained confident about the effectiveness of its products. "What we have here is a dispute between a government agency and industry over what is an effective test," he said.

Because of the disagreements between industry and Florida researchers over the state's test results, the Association of Official Analytical Chemists — a professional organization that sets testing procedures for many drugs and pesticides — is planning a review of germicide tests.

The extent of the health problem caused by ineffective germicides is unknown because little study has been done in the field, according to researchers.

"It's not the primary route of hospital infections," said Barry Davis, an environmental health engineer with the federal Centers for Disease Control. But, he added, "we don't know enough about it to make it a major concern. It's something that should be looked into."

Florida has been testing germicides since the late 1960s, but the failure rate of the products has become significant only in the past 18 months, said Steve Rutz, administrator of the state agriculture department pesticide enforcement section.

The products that failed state tests included:

Adams Sani-Quat, Adams Veterinary Research Laboratory, Miami.

Sterone Air Freshener, Cleaner, Disinfectant, Deodorizer, Fungicide, Virucide; American Disinfectant Cleaner; Arm Medi-Septic Hospital Type Surface Disinfectant, Deodorant; American Refining and Mfg., Inc., Miami.

A-33 Dry, A-500 Detergent Disinfectant, A-3 Detergent Disinfectant, Omega Concentrate Disinfectant; Airwick Industries, Secaucus, N.J.

Auto-Chlor DS-33 Disinfectant, Auto-Chlor Systems, Memphis, Tenn.

Barrier Conquest, Barrier Industries, Port Jervis, N.Y.

Steri-Zone Disinfectant, Biscayne Chemical Laboratory, Miami.

Butcher's Clockwork Disinfectant, Deodorizer, Sanitizer; Butcher Polish Company, Marlborough, Mass.

Duke Hospi-Septic, Duke Industries, Hialeah.

Hava-Tampa Emerald Pine Scented Disinfectant Deodorizer; Eli-Witt Company, Tampa.

Fort Dodge Nolvasan S Scented, Fort Dodge Laboratories, Fort Dodge, Iowa.

Lemon Scented Disinfectant, Gator Chemical, Largo.

Hi-Tor Germicidal Detergent, Huntington Laboratories, Inc., Huntington, Ind.

Sunicide 256 Concentrated Detergent Disinfectant Fungicide, Lawton Brothers, Inc., Orlando.

Formula NI-765 Disinfectant, Neutron Industries, Torrance, Calif.

Johnson Wax Blue Chip Germicidal Cleaner, S.C. Johnson and Son, Racine, Wis.

Sio-Dex Staph Kill Hospital Disinfectant, Selcol Disinfectant Sanitizer Fungicide, Deodorizer; Selig Chemical Company, Atlanta, Ga.

Sanitizer P Sanitizing Agent, TC 505 Q Hospital Free Germicide Cleaner, Theochem Laboratories, Tampa.

Vesphene II, Vestal Laboratories, St. Louis, Mo.

1982

recognize that defense against attack space.

Hospital Infections' Cost Cited

United Press International

Accidental infections caught by hospital patients kill about 80,000 people each year and add as much as $1.5 billion to the nation's health care costs, according to federal health officials.

William Foege, director of the Centers for Disease Control, said 2 million Americans who enter hospitals each year — 5 percent of all admissions — catch infections unrelated to their original condition.

The accidental infections, he said, lead directly to 20,000 deaths and indirectly to another 60,000. Such infections add an average of four days to a patient's hospital stay, at a total cost of more than $1 billion a year, he said.

The CDC, in testimony before a Senate appropriations subcommittee discussing its budget, reported progress on one front — measles, which it said may be virtually eliminated in the next two years.

Herpes infections, however, continue to defy treatment, the CDC said.

Foege said budget concerns have prevented his agency from working on the problem of herpes.

There are from 200,000 to 500,000 new cases of herpes infections each year and at least 5 million Americans are infected — an 800 percent increase in the last 15 years, Foege said.

About 1,000 children are born to herpes infected mothers each year. Half of these children die and a quarter are mentally retarded.

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STATE OF FLORIDA FLORIDA DEPARTMENT OF AGRICULTURE & CONSUMER SERVICES
DOYLE CONNER COMMISSIONER * MAYO BUILDING TALLAHASSEE 32301

February 18, 1983

Mr. Aran Beloian
T-768-C
Environmental Protection Agency
BFSD, EPA
401 M St., S. W.
Washington, D. C. 20460

Dear Mr. Beloian:

Below you will find the current information which we have concerning the contaminated lot of disinfectant. As soon as the identity of the other organism recently isolated is confirmed, we will transmit this to your attention.

Product: Barrier Conquest 1000 - Hospital Disinfectant (Label attached)

EPA Registration No. 31521-20-8238
EPA Est. No. 8238-NY1

1. Original sample was received 12/2/82 in a pint jar. The original container was a 5 gallon can and the inspector had withdrawn the sample. The sample was determined to be contaminated since 20/20 tubes were positive for Salmonella, Pseudomonas and Staphylococcus.

   Total aerobic plate count = 140,000/ml sample

   Biochemical identification:
   Gram negative rod
   Blue fluorescent pigment
   Gibco Sensititre System:
   Nitrate -
   Glucose +
   Decarboxylase +
   Oxidase +
   Lysine decarboxylase -
   Indole -
   Urease +
   Ornithine decarboxylase -
   Voges-Proskauer -
   Citrate +
   Malonate -
   Tryptophane deaminase -
   Esculin -
   Gelatin Liquefaction -
   Hydrogen sulfide -
   Inositol -
   Mannitol -
   Adonitol -
   Arabinose -
   Maltose -
   Rhamnose -
   Sorbitol -
   Sucrose -

   Identity of organism:
   Biocode 4220000
   Pseudomonas aeruginosa or Pseudomonas cepacio

Since the original sample received was not in the original container, the inspector went back and submitted the 5 gallon can on February 9, 1983. This was also found to be contaminated. When the container was received it was thoroughly rotated to mix the contents before sampling. Enumeration of the bacterial content of the 5 gallon container was 590 organism/ml.

No specific code stamped on the container could be identified. There was a handwritten number on the rim of the container which appeared to be a code. This number was

C23 3463 05 (or) OS

Three pieces of colored tape were on the container: one yellow green, one gold, and one yellow. We have no idea as to their applicability as far as coding might be concerned.

The second sample(the 5 gal container) was found to contain several different types of organism:
1. Gram positive cocci
2. Gram negative rods (presumptive 2 types)

Biochemical testing on these organisms is not complete as of this date. One of the Gram negative rods does possess the fluorescent blue-green pigment characteristic of the original bacterial culture.

Several other comments can be offered concerning this product. The first contaminated sample (5174) was received as a followup sample to sample 1 which was found ineffective against Pseudomonas (16/30+). This first sample was not contaminated. An additional subsequent sample 5871 was also found ineffective against Pseudomonas (26/40+). Presently no other lots have been found to be contaminated with viable microorganisms.

The original report was made to state and EPA enforcement officials here in Florida and the EPA officials in Region IV and Washington. We will notify all parties of any further subsequent identification of contaminating organisms.

A summary table of all samples and results is attached for your review. If we can furnish any further information concerning this, please contact me.

Sincerely,

Martha E. Rhodes, Ph. D.
Chief, Food Laboratory
DIVISION OF CHEMISTRY

CC: Dr. C. H. Van Middelem
Vincent Giglio
Steve Rutz
Bruce Miller
Jim Downing
Marshall Gentry
Dr. Reto Engler
Dr. Stephen King
Dr. A. W. Tiedemann, Jr.
Dr. Singh Dahiya
Mr. Alvin Burger

Barrier Conquest 1000 - EPA Registration No. 31521-20-8238

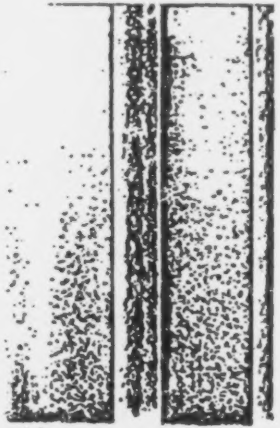
Food Lab No.	Pesticide No.	Container	Color of sample	Analytical findings
1	44229	glass jar rec'd 7/1/82 Tested @ 1:128 325ppm	Blue green	Pseudomonas 16/30+ Salmonella 0/10+ Staphylococcus 0/10+ Trichophyton ---
5174	47340	glass jar rec'd 12/2/82 Tested 1:128 325 ppm	Yellow	All organisms 20/20+ Contaminated with 140,000 organisms/ml Identified as P. aeruginosa or P. cepacio
5871	23-1097 (Div. of Purchasing)	Orig. 1 gal Rec'd 1/10/83 Tested 1:128 325 ppm serum	Blue green	Pseudomonas 26/40+ Salmonella 0/10+ Staphylococcus 1/20+ Trichophyton +-- No viable organisms detected
6629	48383	glass jar rec'd 2/9/83	Blue green	No viable organisms detected Use dilution & funcidical procedure not complete
6830	48458	Orig. 1 gallon Rec'd 2/11 /83	Blue green	No viable organisms detected Use dilution & fungicidal procedure not complete
6831	48459	Sterile whirl-pak Rec'd 2/11/83	Blue green	No viable organisms detected Use dilution & fungicidal Procedure not complete
6689	47340	Orig. 5 gal Recd 2/9/83 Tested 1:128 325 ppm serum	Yellow	All organisms 20/20+ Product contaminated with 590/ml viable bacteria Gram + cocci & Gram - rods

Note: Contaminated samples were yellow in color excellent wetting and penetrating properties of CONQUEST 1000 ides rapid removal of al' kinds of soil, is safe for all washable surfaces leaves no surface-dulling film.

QUEST 1000 is a highly effective deodorizer. It emulsifies odorous ic matter and destroys odor-producing organisms.

RNING: Harmful if swallowed. Causes skin and eye irritation. Do not get es, on skin, or on clothing. Care should be taken in handling the ntrate, including proper shielding of eyes in case of splashing. Use er gloves for manual cleaning operations. Avoid contamination of food.

T AID: In case of contact with eyes, immediately flush eyes with plenty er for at least 15 minutes and get medical attention. If contact with skin s, flush immediately with plenty of water. Remove and wash minated clothing. If swallowed, drink promptly a large quantity of milk, whites, gelatin solution or if these are not available drink large quantities ter. Call a physician immediately.



BARRIER CONQUEST 1000

BROAD SPECTRUM DISINFECTION

Cleans and disinfects in a single step application.
An excellent detergent system for effective cleaning.

• DEODORIZES • PREVENTS MOLD AND MILDEW • STAPHYLOCIDAL
• PSEUDOMONACIDAL • TUBERCULOCIDAL • FUNGICIDAL • VIRUCIDAL*

AOAC PHENOL COEFFICIENTS	
Staph. aureus (ATCC No. 6538)	10
Salmonella typhosa (ATCC No. 6539)	10

ACTIVE INGREDIENTS	PERCENT
Potassium o-Benzyl-p-chlorophenate	3.962%
Potassium o-Phenylphenate	3.914%
Sodium Dodecylbenzenesulfonate	1.200%
Tetrasodium Ethylenediamine Tetraacetate	1.140%
INERT INGREDIENTS	89.784%
	100.000%

CCEPTED FOR
REGISTRATION
G. M. GENTRY

Net Contents: Gallon(s)

WARNING

KEEP OUT OF REACH OF CHILDREN. SEE LEFT PANEL FOR ADDITIONAL PRECAUTIONARY STATEMENTS AND FIRST AID.

SOLD BY

~~BARRIER CHEMICALS INC./VERNON, NEW JERSEY 074~~ [redacted]

1549

1. DIRECTIONS: For disinfecting and cleaning walls, floors and other smooth hard surfaces, use (1) one oz. CONQUEST 1000 per gallon of water. Apply with a mop, sponge or cloth. Rinsing is optional.

For heavily soiled areas, use (2) two oz. CONQUEST 1000 per gallon of water. Treated food contact surfaces must be thoroughly scrubbed with detergent and rinsed with potable water prior to reuse. Rinse empty container thoroughly with water and discard it.

0933A

To insure accurate solution and portion control, this concentrate should be used with Barrier's One Stroke Dispenser. Each dispenser stroke [illegible] will measure out 1 oz. of concentrate per gallon of solution to be prepared. One oz. requires one stroke, two oz. require two strokes.

6573

7003

CONQUEST 1000 is an excellent disinfectant for use in hospitals, nursing homes, sanitariums, schools, homes, motels, hotels, terminals, offices and rest rooms. Its broad spectrum disinfectant action is proven effective against a wide range of both gram-positive and gram-negative bacteria including Staphylococci, Pseudomonas, TB bacilli, and many enteric organisms, as well as pathogenic fungi. Retains disinfectant effectiveness in the presence of organic matter and hard water up to 325 ppm hardness as CaCO3 (Calcium Carbonate).

*Virucidal against Herpes Simplex (a member of the virus family that causes infectious mononucleosis), Vaccinia (representative of the pox viruses) and Influenza A2 (the Hong Kong flu virus) on inanimate environmental surfaces.

TO CONTROL MOLD AND MILDEW on hard nonporous surfaces, Use (1) one oz. CONQUEST 1000 per gallon of water. Apply this solution with a mop, sponge or cloth so that surface is thoroughly clean and moistened. Do not rinse. Repeat application when new growth appears to maintain control.

EPA Reg. No. 31521-20-8239
EPA Est. No. 8239-NJ-1
NY

MAR 2 1 1979

DEC 1 3 1979

DEC 1 0 1980

DEC 9 1981

DEC 2 0 1982

March 23, 1983

Dr. Marshall Gentry
Florida Dept. of Agriculture
and Consumer Services
Division of Chemistry
Mayo Building
Tallahassee, Florida 32301

Dear Dr. Gentry:

The Office of Pesticide Programs of the Environmental Protection Agency decided that all pesticide products (hospital disinfectants, insecticides, herbicides etc.) used in agriculture, homes and gardens, hospitals, etc. do not need to be tested for effectiveness or safety, because marketplace economics will regulate the industry.

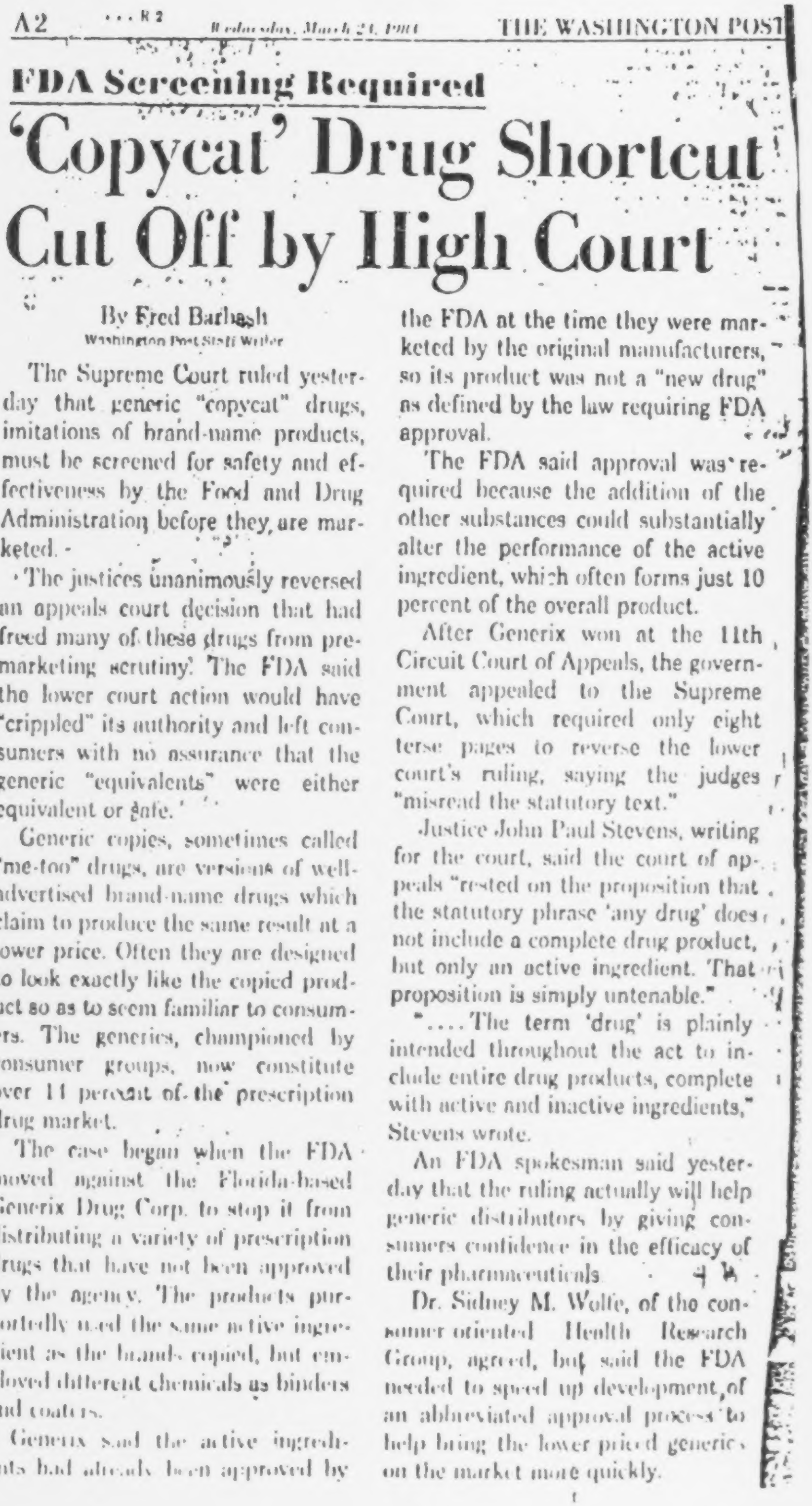
The Supreme Court ruled on March 5, 1983 that generic "copy cat" drugs, imitations of brand name products, must be screened for safety and effectiveness by the Food and Drug Administration.

Should not the same reasoning hold true for these highly toxic pesticide chemicals which are formulated by the thousands of me-too type pesticide formulators and manufacturers.

If you agree with this viewpoint, please contact your congressional representative or senator and advise them to support the proposed admendment as introduced by Senator Sarbanes as indicated on the enclosed attachment.

Concerned EPA Employees

Enclosure



A2 . . . R2 Wednesday, March 23, 1983 THE WASHINGTON POST

FDA Screening Required

'Copycat' Drug Shortcut Cut Off by High Court

By Fred Barbash

Washington Post Staff Writer

The Supreme Court ruled yesterday that generic "copycat" drugs, imitations of brand-name products, must be screened for safety and effectiveness by the Food and Drug Administration before they are marketed.

The justices unanimously reversed an appeals court decision that had freed many of these drugs from premarketing scrutiny. The FDA said the lower court action would have "crippled" its authority and left consumers with no assurance that the generic "equivalents" were either equivalent or safe.

Generic copies, sometimes called "me-too" drugs, are versions of well-advertised brand-name drugs which claim to produce the same result at a lower price. Often they are designed to look exactly like the copied product so as to seem familiar to consumers. The generics, championed by consumer groups, now constitute over 11 percent of the prescription drug market.

The case began when the FDA moved against the Florida-based Generix Drug Corp. to stop it from distributing a variety of prescription drugs that have not been approved by the agency. The products purportedly used the same active ingredient as the brands copied, but employed different chemicals as binders and coaters.

Generix said the active ingredients had already been approved by the FDA at the time they were marketed by the original manufacturers, so its product was not a "new drug" as defined by the law requiring FDA approval.

The FDA said approval was required because the addition of the other substances could substantially alter the performance of the active ingredient, which often forms just 10 percent of the overall product.

After Generix won at the 11th Circuit Court of Appeals, the government appealed to the Supreme Court, which required only eight terse pages to reverse the lower court's ruling, saying the judges "misread the statutory text."

Justice John Paul Stevens, writing for the court, said the court of appeals "rested on the proposition that the statutory phrase 'any drug' does not include a complete drug product, but only an active ingredient. That proposition is simply untenable."

". . . . The term 'drug' is plainly intended throughout the act to include entire drug products, complete with active and inactive ingredients," Stevens wrote.

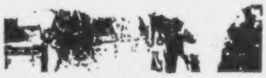
An FDA spokesman said yesterday that the ruling actually will help generic distributors by giving consumers confidence in the efficacy of their pharmaceuticals.

Dr. Sidney M. Wolfe, of the consumer oriented Health Research Group, agreed, but said the FDA needed to speed up development of an abbreviated approval process to help bring the lower priced generics on the market more quickly.

Dick Bray, new ASM Meetings Director, holds an amiable corridor consultation with Dr. Robert C. Moellering, Jr., ICAAC Chairman.

tions reached an all-time high of 161 booths.

"There was a heavy representation by pharmaceutical companies, particularly in the diagnostic field. Every new and different product available to the microbiologist and infectious disease specialist



Picturesque Bourbon Street in New Orleans, site of the ASM's 83rd Annual Meeting, March 6-11.

CDC Study Provides latest Information on Nosocomial Infections

A national study by the Centers for Disease Control has shown that nosocomial infections with *E. coli, K. pneumoniae,* and *P. aeruginosa* resistant to gentamicin or tobramycin cause death more often than those with susceptible strains.

Describing the report on National Nosocomial Infections Study in which hospitals conduct total surveillance of nosocomial infections, Dr. J. Hughes of the CDC in Atlanta emphasized that "infections most often causing death should be a high priority for surveillance and control efforts."

Between 1975 and 1981, an average of 72 hospitals reported data on nosocomial infections to the CDC yearly, he commented. During those seven years, 21,056 deaths occurred among patients with a total of 88,433 nosocomial infections.

"Deaths were most frequently associated with infection on medical services, followed by surgery, pediatrics, and newborn," Dr. Hughes reported. "The fatality ratio associated with pneumonias was greater on medicine than on surgery. Infections associated with 2° bacteremia had three times the fatality ratio of those without bacteremia."

Epidemiology Assessed

Among infected patients, it was found that 14 percent of deaths were caused by nosocomial infections. The proportion of deaths caused by nosocomial infections was greater on pediatric/newborn than on medical/surgical services. Nosocomial infections caused death most often in CNS and intra-abdominal infections, 1° bacteremia, and pneumonia, Dr. Hughes added.

In another report, the unusual epidemiology of nosocomial infections in a children's hospital was described by Dr. R. Welliver of SUNY and Children's Hospital in Buffalo, N.Y.

"The epidemiology of these infections in children's hospitals is unique in comparison to other types of institutions," Dr. Welliver observed. "The considerable morbidity and rare mortality of viral nosocomial infection is underestimated by surveillance programs focusing on bacterial infections."

Dr. Welliver calculated the incidence of bacterial and viral infections in a large children's hospital over a 12-month period. The annual attack rate for nosocomial infections for the hospital as a whole was 3.2 percent. As expected, high attack rates were observed in the intensive care nursery and pediatric ICU. Attack rates on infant floors were over twice those on other floors.

"In contrast to studies in general hospitals, respiratory and gastrointestinal tracts were the most common sites of nosocomial infection," Dr. Welliver observed. "Staphylococcus aureus was the pathogen most often responsible for the infections, with rotavirus the next most common. Infants and patients on neurosurgical services were particularly prone to viral nosocomial infections."

Nosocomial Eye Infections

Another New York investigator reported that nosocomial eye infections represent an often unrecognized, potentially serious nosocomial hazard, particularly in the obtunded, intubated patient with pneumonia. In an 18-month period, eight patients in three separate ICUs were noted to have nosocomial eye infections, Dr. E. Hilton of Montefiore Hospital and Albert Einstein College of Medicine, Bronx, N.Y.

"The infections were noted solely by nurses in three of the eight cases," he emphasized. "Appropriate therapy was given to four patients. Complications of the infections included corneal rupture, opacification or thinning in four cases, and four patients died."

Observation of tracheal suctioning technique and patient positioning suggested that left eye involvement resulted from contamination during suctioning.

Cohort System Recommended

Another investigator described epidemic gentamicin-resistant *Klebsiella pneumoniae* in a neonatal intensive care unit. According to D. L. D. Saravolatz of Henry Ford Hospital in Detroit, Mich., the most effective control measure was the utilization of a strict cohort system which prevented both infection and colonization with the epidemic strain.

Nosocomial septicemia with coagulase-negative staphylococci in a neonatal intensive care unit was the subject of a report by Dr. A. Fleer of Wilhelmina Children's Hospital in Utrecht, The Netherlands. Dr. Fleer concluded that CNS contaminated total parenteral nutrition solutions may be a source of CNS septicemia in premature newborns.

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I Conf on Antimicrobials & Chemotherapy

HIGHLIGHTS ISSUE OF THE 22nd

AUG 17 1983

two to four fluid ounces product in one gallon of water per 100 pounds of seeds to be treated; one seed application only; residues of imazilil and its metabolite alpha-(2,4-dichlorophenyl)-1H-imidazole in or on blackeye beans is 0.2 p.p.m.; expires Aug. 1, 1983.

--To the California Department of Food and Agriculture for use of glyphosate to control johnsongrass, Bermuda grass and field bindweed in kiwi fruit. Use of the product Roundup, manufactured by Monsanto Co., may be applied; a maximum of two ground applications at a maximum rate of 3 lbs. active ingredient (three quarts) per acre; a 60-day pre-harves interval; a total of 16,200 lbs. active ingredient will be used to treat a maximum of 5,400 acres of kiwi fruit; maximum residues are 0.1 p.p.m.; exemption expires April 26, 198

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EPA APPROVES $10 MILLION FOR STRINGFELLOW CLEAN-UP ACTIVITIES

EPA has agreed to a $10 million Superfund expenditure to clean-up the Stringfellow hazardous waste site near Riverside, Calif., according to an August 2 EPA press release.

The agreement signifies EPA approval of California's clean-up plan for the site. The decision follows policy lines set by the agency to move ahead with clean-up efforts while enforcement efforts are still pending. The Stringfellow suit was filed by the Justice Department on behalf of EPA, asking for cleanup costs of $20 - $40 million, last April after industry parties and the agency failed to reach an agreement to clean-up the site. The suit is still pending (See April 27, Page 14).

The $10 million will be used to investigate site conditions, provide additional fencing and security, control erosion, and to continue off-site disposal of leachate from the site, EPA said. The initial efforts will also include a feasibility study, to be managed by EPA, on options for controlling the groundwater plume beneath the site, according to the agency press release. The feasibility study, which is expected to take 18 months, is also expected to examine long-term cleanup options including treatment in place and removal of wastes.

An EPA spokesman explained the $10 million will be given out in parcels because the Superfund dollars are running out for this fiscal year. During the next eight weeks, EPA plans to spend approximately $3 million on the initial control efforts and the feasibility studies. Later funding will include reimbursing the state for money it has already expended in cleaning up the site and money spent on emergency actions when heavy rains caused ponds on the site to overflow.

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AMERICAN SOCIETY FOR MICROBIOLOGY QUESTIONS EPA END TO BIOLOGICAL TESTING

The American Society for Microbiology has written to EPA Administrator William Ruckelshaus asking why pre- and post-registration efficacy testing of chemical disinfectants and sterilizers was terminated by the EPA OPP last summer without public notice or explanation.

In a July 22 letter, The Society's Public and Scientific Affairs Board said termination of the program "has important public health implications that may not have been fully explored. . ."

"Because the success of all microbiological research and of our professional services depends in part on the efficacy of chemical disinfectants and sterilizers, we are compelled to ask how pre- and post-registration testing is now performed and how the EPA plans in the future to provide assurance that chemical disinfectants and sterilizers will be effective if used as directed on the label?" the group asked.

It also asked whether EPA is considering alternatives to intramural efficacy testing. contending that registration of bactericides, fungicides, sporicides and virucides cannot be based solely on data generated by the manufacturer in support of label claims or depend only on information obtained from non-federal laboratories on a contractural basis.

Ruckelshaus Indicates to Sarbanes He will Not Reverse Decision to Close Lab

Meanwhile, Ruckelshaus discussed the issue of efficacy testing and the closure of the laboratory in Beltsville, Md., which had conducted the biological tests, recently with Sen. Sarbanes (D-Md.). Sarbanes is the author of a bill to require EPA to maintain an independent lab to verify biological test results.

According to staff members at both EPA and on the Hill, Ruckelshaus would not give Sarbanes a commitment to reverse the decision made last summer, but said he would look into the issue further to determine if agency officials are proceeding with a program to contract out such testing on an as-needed basis.

Sarbanes expressed dissatisfaction with this arrangement, according to a staff member and noted that in the past year no such contracts have been let.

The staffer said Sarbanes does not intend to drop the issue.

o

NO STATE RCRA PROGRAMS REVERT TO EPA AFTER JULY 26 DEADLINE

No state RCRA programs reverted to EPA on the July 26 deadline for completion of interim authorization applications. Most of these, 37 states, received extensions from the agency.

Notices of these extensions in the Federal Register set individual dates for each state to meet a final authorization deadline, with intervening schedules for drafts and different phases of application (See July 27, Page 23). EPA's summary of the extensions said, "Extensions range from a two months (for Delaware) to one and one-half years (for New Jersey and Puerto Rico). The average extension is approximately nine months."

Only three of the states, Miss., Okla., and Conn., met the July 26 deadline by completing applications and receiving interim authorization for both Phases of the RCRA program.

While the July 26, 1983 deadline applied only to state completion of applications for interim status, the January 26, 1985 final authorization deadline applies to EPA approval of the state programs.

Five states, Michigan, Minnesota, Colorado, South Dakota and Idaho, are listed on EPA's tally as skipping interim authorization and moving directly to final authorization. EPA also listed two states, Wyoming and Hawaii, and three territories, American Samoa, Virgin Islands, and Northern Mariana Is., which are not expected to apply for authorization of any portion of the RCRA program.

The status of several states is unique. New York, for example has applied for Phase I interim authorization but it has never been granted by EPA. In such an instance there is no state program to revert, but the state has not met the July 26 deadline for applying for interim authorization for either Phase I and II of the RCRA program, according to EPA's summary.

o

Jim Downing

Administration halts EPA disinfectant tests

3/6/83 BALTO SUN, SUN

By Vernon A. Guidry, Jr.
Washington Bureau of The Sun

Washington — The Reagan administration has put an end to an Environmental Protection Agency biological testing program that had been turning up high rates of failure in testing the effectiveness of disinfectants used by hospitals.

EPA has gone to other means of checking the disinfectants, but officials acknowledge their system is not completely in place, even though the agency began cutting back its in-house testing program in 1981.

Critics maintain there is no substitute for the independence, expertise and experience of the EPA biological testing laboratory in Beltsville, where the difficult procedures involved in biological testing were carried out

In defense of the action, EPA pesticides chief Dr John A. Todhunter said last year that in the interest of efficiency, tests already conducted by manufacturers should not be repeated at Beltsville.

"In this instance, we must rely on the integrity of manufacturers and the laboratories which they may employ to perform . . . tests and the interest of the user community in assuring efficacious products," he said.

Although the issue has been smoldering for more than a year, it has received little attention outside the industry, even among users. A spokeswoman for the American Hospital Association in Chicago said yesterday that the organization was not aware of high failure rates in disinfectants subjected to EPA testing.

That is beginning to change as EPA comes under scrutiny over allegations that it has gone too far to accommodate industry on a number of environmental and health issues. For instance, the March issue of a small trade publication, *Hospital Infection Control*, asks in its lead story: "Who guarantees that the disinfectants in your hospital are efficacious?"

The answer the publication comes up with is, for the most of the nation, no one.

'83 MAR -8 A11:59

The EPA mantains that it is doing the job, but state officials, scientists and Senator Paul S. Sarbanes (D, Md.) challenge that assertion.

Mr. Sarbanes said at week's end that the decision to halt disinfectant tests as well as biological testing on the effects of other pesticides at Beltsville was "outrageous and raises serious questions aout the EPA's ability to comply with its responsibilities to the people for the protection of the environment."

The disinfectants in question are used to kill infection-causing bacteria in hospitals, nursing homes and other health-care facilities.

According to a former EPA employee and to an account in the trade press, as many as 50 percent of the hospital disinfectants tested at Beltsville failed to meet effectiveness standards.

Warren R. Bontoyan, chief of the EPA laboratories in Beltsville, says he does not recall the exact figure. "It was pretty high. Probably in the area of 30 to 40 percent."

James G. Touhey, director of benefits and field studies in EPA's pesti-

See DISINFECTANT, A21, Col. 1

NCA, FRUSTRATED WITH EPA OVER TOXAPHENE DISPOSAL TAKES MATTER TO BUSH

EPA's inconsistent and non-existent answers to the probiem of disposal of toxaphene livestock dips propelled the National Cattlemen's Association (NCA) to take the matter to Vice President George Bush and his Task Force on Regulatory Relief (See June 29, Page 26). NCA outlined the problem beginning in 1979 to the present, including the decision of last month to abandon consideration of an exemption to RCRA regulations which would have given "larger, commercial users of toxaphene the option of disposal by land spreading."

The NCA letter, sent earlier this month by NCA President, William J. Waldrip, noted that after the association was informed about the consideration of a RCRA exemption, NCA asked for a meeting with EPA officials to try to resolve the toxaphene disposal problem.

Officials told NCA at the meeting that the exemption was currently impossible, and that the options were:

"1) That industry and/or the states hire a consulting firm to draft an exemption from RCRA; the time required would range frcm 2-6 months for drafting and two years for EPA review and drafting. EPA does not have the necessary staff to prepare the proposed exemption;

"2) Suggest that dip vat operators apply with Region VIII for RCRA disposal permits, which is admittedly time consuming and expensive;

"3) Dispose of toxaphene in approved hazardous waste sites -- most states do not have them."

NCA noted that between Feb. and July 1983, members have found dip in short supply with no improvement immediately because EPA has not approved revised labels and that EPA Region VIII has "periodically called state veterinarians and inquired when the state(s) are going to discontinue the use of toxaphene. The South Dakota Livestock Sanitary Board discontinued the required use of toxaphene in May due to violation notices issued to two livestock markets."

The letter has been sent to EPA for reply, not received by NCA at press time.

NCA also noted that EPA has not yet responded to Wyoming's Dec. 23, 1982 request for a hearing on the notice of intent to cancel or restrict registration for toxaphene.

Nor has the agency responded to NCA's request for consideration of disposal of spent dip containing toxaphene on grazing land, according to the material sent to Bush.

●

EPA EXPLORING OPTIONS FOR DEALING WITH DISINFECTANT EFFICACY

EPA has not abandoned responsibility for disinfectant efficacy entirely (See March 9, Page 30; and April 13, Page 12). Illustrations of agency involvement in the matter are in an Aug. 18 letter to Dr. Robert P. Williams, President, American Society of Microbiology, from Don R. Clay, Acting Assistant Administrator for Pesticides and Toxic Substances, EPA. These included:

-- Examination of the possibility of using mechanisms similar to those applied by FDA to antibiotics and color additives; that is batch certification and plant inspections for disinfectants.

-- Willingness to evaluate any constructive alternatives from any quarter to assure disinfectant efficacy.

-- Exploring with the Association of Official Analytical Chemists (AOAC) its "involvement in a testing laboratory certification program."

-- Encouraging but not requiring "registrants to submit data on the minimum effective dose of a product, or the use dilution at which the product approaches a failure of the AOAC use dilution test for use or one or more organisms."

-- Phasing out of the Beltsville efficacy screening program should focus attention on how disinfectant efficacy assurance can be most effectively achieved.

-- The agency is contributing to refinement of the use dilution test and to reduction of its variability.

Clay said EPA is "concerned about the public health implications of disinfectant efficacy, but we are convinced that EPA cannot be the sole focal point for assuring that public health will not be endangered by ineffective products."

His letter stated, "We decided to phase out routine efficacy screening because we believe the Beltsville program may have created a false sense of security among the general public and the users." It continued:

> "This stems from the common misconception that EPA screened each and every disinfectant product proposed for registration or already in the marketplace. However, in fact, preregistration screening was carried out only infrequently, and for enforcement purposes, only a limited number of batch samples were selected from the many products available in the marketplace. For example, there are approximately 3,300 hospital use disinfectant products registered with EPA, and thousands of batches of each product are produced annually. However, in 1981 and 1982 only 80 batch samples of hospital disinfectants were screened by the Beltsville laboratory for post-registration enforcement purposes. This is only a minute percentage of all the products available. Similarly because the program was being phased-out, 1982 preregistration screening was limited to less than 10 studies. I am sure you would agree that this was a less than thorough effort to assure efficacy.
>
> "Administrative and resource factors also played a significant role in the decision to phase-out disinfectant testing. We believe that the personnel assigned to the task were not being optimally utilized. Thus, the personnel were transferred to other positions where their skills could be more fully used to contribute to other, higher priority goals. However, the laboratory facility itself has not been closed, and we have been maintaining cultures of microorganisms there for use on an as-needed basis. We are in fact resuming some very limited testing to support EPA regional office enforcement activities and state activities."

The EPA official observed, "having removed the 'security blanket' of federal disinfectant testing, we presumed that private sector groups, principally the American Hospital Association and other professional groups, would have an interest in undertaking a credible testing program, but to date, little interest has been demonstrated. Though cognizant of the problem, individual hospitals do not appear to have adequate resources or the inclination to become involved."

●

HOSPITAL INFECTION CONTROL
67 Peachtree Park Drive, N.E. / Atlanta, Georgia 30309
Telephone: 404/351-4523

See p 29

HOSPITAL INFECTION CONTROL
PRESENTING THE LATEST NEWS AND COMMENT IN THE FIELD OF HOSPITAL INFECTION CONTROL
VOLUME 10/NUMBER 3 (pages 29-40) MARCH 1983

Do disinfectants need tests for effectiveness?

Who guarantees that the disinfectants used in your hospital are efficacious?

Unless your hospital is located in Florida, North Carolina or Virginia, no one is verifying by tests the manufacturers' statements that the disinfectants actually kill the organisms they claim to kill. The few tests being done appear to show failure rates of from 12% to 50% in the samples tested. Most states, however, do check to determine if the product contains the ingredients listed on the label.

Disinfectants are considered pesticides, and the U.S. Environmental Protection Agency regulates them.

Until about a year ago, the EPA's laboratory in Beltsville, MD, used microbiological and chemical tests to see if the disinfectants actually worked.

One EPA source there told HIC that about 50% of the disinfectants checked failed the tests. But the testing program was eliminated by the current administration.

EPA registers disinfectants

The EPA still registers disinfectants, and, to earn the registration, a manufacturer must submit data showing his product can meet its label claims. However, the only check of those data is done by "a person at a desk."

RETO ENGLER, PhD, chief of the EPA's disinfectant division, said that currently the EPA favors testing programs on the state level. "There is a need [for testing], but the question is whether the need is at the state level or at the federal level. The present trend is that the state level is favored for regulation."

However, only three states have testing programs, and two of those are minimal programs. None of the states tests to determine the efficacy of sporicidal disinfectants.

Florida has active testing program

The most active state program is in Florida, and is headed by microbiologist **MARTHA RHODES**, PhD, chief of the microbiology section of the food laboratory within the Florida Department of Agriculture and Consumer Services.

Rhodes told HIC that about 12% of the products tested there failed.

The products are tested according to AOAC (Association of Official Analytical Chemists) specifications. Those specifications include a "use-dilution" test to simulate in-use killing power, a glass slide spray test which simulates use of an aerosol, and tests for fungicidal activity.

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- Guidelines for wearing OR garb 34
- Nosocomial meningitis 36

"We use the AOAC or any modification which the EPA has given us," Rhodes said.

If the products fail after repeat testing, the state's Pesticide Enforcement Section of the agriculture department is notified. **STEVEN RUTZ**, administrator of that section, said the department first notifies the user of the product. The department tells the user, such as a hospital, of its findings, and it is up to the user to decide whether to continue using the product or to contact the manufacturer.

Department tells manufacturer of failure

The department also notifies the manufacturer that it is in violation of the Florida pesticide law. "We tell them this product was misbranded because it failed to kill this test organism which it should, according to what is on the label," Rutz said.

Beginning January 1, the state could also impose penalties on the manufacturers for inefficacious disinfectants. But the rules for the new law have not been written. As soon as they are, Rutz said the state may impose penalties of up to three times the invoice price of the product. The penalties would be paid to the consumer. For example, if a hospital found, through state testing, that the products it was using were not effective, the hospital would collect the penalties imposed.

EPA can also investigate

The state can also "forward the case to the U.S. EPA for consideration or action. This hasn't happened recently because of the disagreement over the testing methods," Rutz said.

Rutz also said the state is not taking either action because it has decided to do some collaborative testing with the manufacturers on the methods.

"We cannot account for the differences in results presently being found in laboratories used by the state of Florida and the companies. We also recognize that this is a complex scientific problem that we intend to resolve," said **RALPH ENGEL**, president of the Chemical Specialties Manufacturers Association (CSMA), Washington, D.C., which represents most manufacturers of disinfectants.

"We do not believe the products are ineffective. We think there is a problem with the test methods, procedures, equipment, organisms used or all of these things," Engel said.

"We have set up a task force that includes representatives from Florida, the EPA, the CSMA, and the AOAC to review the test methods and tighten where possible. We want to tighten as many variables as possible, recognizing that dealing with a biological test you always have some variables. The objective is to tighten controls and reduce the variablity in the testing procedure," he commented.

Tests developed as cooperative effort

DAVID B. MacLEAN, PhD, executive director of the AOAC, explained that the U.S. Department of Agriculture and the CSMA developed as a cooperative effort, most of the methods used to test disinfectants in the 1960s.

"Starting about two years ago, we began to get some concerns expressed" about the test methods. The EPA and the Florida state lab, employing the use-dilution test, found that some products don't work, he said. "They don't kill

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bacteria. They have the ingredients on the label, but they don't do the job."

MacLean said that **GAYLE MULBERRY** has been named associate referee of the use-dilution test. He will look at the test and consider making editorial changes in the written procedure guide or changing the method.

AOAC requires collaborative study of tests

If the method needs changing, AOAC requires a collaborative study involving at least six laboratories.

"We look at the tests to see if they are well enough designed and detailed enough so that they can be used in most laboratories without a large amount of skill and imagination," MacLean said.

He explained that with the current use-dilution test a person does not get "good results" if he does it one day and then not for a year.

Practice needed to get consistent results

"You get more consistent results with practice," MacLean commented.

Mulberry, general manager and technical manager of microbiology at Hilltop Labs, an independent testing laboratory, said "There may be some ambiguities in the way the test is written. It gives you too many options of what you can or cannot do. Because of these variations, people interpret the method differently."

For example, Mulberry said the laboratory doing the test can chose the media for growing the organisms. The choice of media may make a difference in how the organisms respond to the disinfectants--whether they live or die in the disinfectant.

Problem is not the failures

EPA's Engler indicated the testing methods were the probems, not the failures. "Unfortunately, we test all the products by just one standard--the AOAC standard. This standard is not a quantitative standard. It is qualitative one. Either the product passes or it fails. But nobody knows how far away from failure this product is formulated. We don't know the minimally effective dose of all these products."

The EPA disinfectant chief, who also works with the AOAC, said levels of disinfection are needed. "I think the hospitals should get involved and say where they want to be 100% sure that no organisms are present and where they just want to be sure that they have done an adequate cleaning or sanitizing job. We call all these products disinfectants, whether they are used to clean a hospital corridor or a medical instrument."

Scientists don't provide guidance

The scientific community doesn't provide clear guidance on product labeling, saying if the product should be used only to clean floors or if it should be used for more critical items, Engler commented.

"We don't provide a clear distinction. More or less, this is everyone's fault because we have never had the guts to address it, because we have never said there is a difference in disinfectants--a quantitative difference," he concluded. ■

AOAC sets methods for testing effectiveness of disinfectants

How are disinfectants checked to see if they can kill bacteria?

The most commonly used test is the Association of Official Analytical Chemists' use-dilution test.

GAYLE MULBERRY, general manager and technical manager of microbiology at Hilltop Labs, Cincinnati, OH, and an AOAC associate referee, explained how the use-dilution test is conducted.

A use-dilution is made according to the package instructions. Ten test tubes containing one-ml of the use-dilution are prepared. Then a stainless steel cylinder, like the cylinders used for antibiotic assays, is inserted into each tube.

Three organisms used in test

The cylinders carry the three test organisms: Staphylococcus aureus, Salmonella choleraesuis and Pseudomonas aeruginosa. If a disinfectant is "hospital strength," the Environmental Protection Agency requires that it kill all three organisms.

The organisms on the cylinders are left in the use-dilution for 10 minutes. After removal, the organisms are subcultured into a medium that neutralizes the disinfectant. The organisms can then be subcultured again to be sure none can still grow.

"The EPA requries 60 replicates (60 carriers of the organisms) and three samples of the product (from three lots of the product). One of the lots must be at least 60 days old," Mulberry noted. ■

Blood banks take tentative steps to prevent AIDS transmission

Blood banks and some plasma collection corporations are initiating policies that they hope will limit the possiblity of transmitting the acquired immune deficiency syndrome (AIDS) to transfusion recipients and hemophiliacs.

Eight hemophiliacs and one child who received several transfusions have been among those who reportedly have the new disease AIDS.

Although researchers are not yet sure how the disease is transmitted, some suspect that an etiologic agent of AIDS is infectious. And there is some concern that the disease may be transmitted by blood and blood products.

Because of those concerns, the American Association of Blood Banks (AABB) recently announced recommendations designed to address the concerns about AIDS related to blood transfusions.

The AABB worked with the American Red Cross and the Council of Community Blood Centers in developing the recommendations.

Blood banks to question donors

JOSEPH BOVE, MD, professor of medicine at Yale University School of Medicine, New Haven, CT, and chairman of the AABB's committee on transfusion of transmitted diseases, told HIC what the group recommends.

Before blood banks accept donations, personnel are to ask donors several questions, such as if the person has lost weight, has had unexplained fever or has had swollen lymph glands. The questions are designed to detect possible AIDS symptoms or exposure to patients with AIDS. However, the group felt that specific questions about a donor's sexual preference were inappropriate and ineffective in eliminating donors with AIDS. Most AIDS cases have occurred in homosexual men.

The recommendations also include the following:

- Advising blood banks to extend to physicians educational campaigns regarding possible transfusion risks.
- Increasing the use of autologous transfusions, especially in elective surgery.
- Preparing for increased requests for cryoprecipitate for use as an alternative treatment to Factor VIII for hemophiliacs.
- Avoiding specific recruitment of groups at high risk for AIDS such as homosexual men and Haitians.
- Working with the leadership of groups which include some individuals at high risk for AIDS.

Since there is no specific test for AIDS, no routine laboratory screening program was recommended by the group.

Another organization concerned about AIDS is the National Hemophilia Foundation.

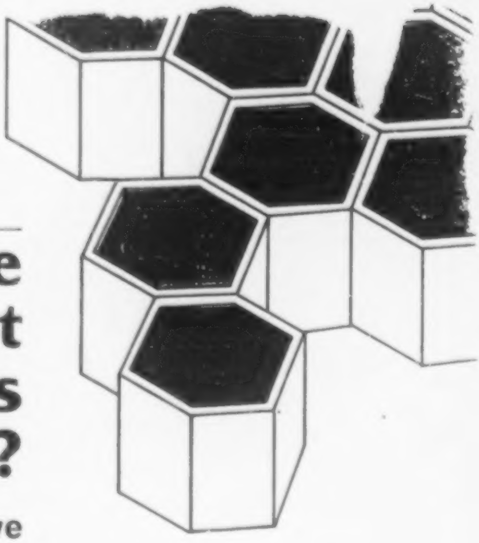
The NHF has suggested that an educational campaign be undertaken so that members of high-risk groups refrain from donating blood.

LEON HOYER, MD, chairman of the NHF medical and scientific council, also noted that when possible, hemophiliacs should use cryoprecipitate since it comes from one donor. Factor VIII is made from pooled plasma.

No cases of AIDS have been linked with cryoprecipitate. The hemophiliacs who have AIDS have all received Factor VIII, but not products from the same lots. ■

Antibiotic review conference focuses on new, costly drugs

The development and marketing of new antibiotics such as the third-generation cephalosporins raises new issues about the risks, benefits, and expenses of



DISINFECTANT TESTING

Are Current Tests Adequate?

The States' Perspective

By Martha E. Rhodes
Chief, Food Laboratory
Division of Chemistry
Florida Department of Agriculture
and Consumer Services

It would be beneficial perhaps to start this article with some background about our testing program in Florida and other states. Our department in Florida is composed of 11 divisions (Table 1) of which the inspectional force is within the Division of Inspection and the analytical laboratory personnel are within the Division of Chemistry. Table 2 demonstrates a further breakdown of the Division of Chemistry and shows the eight line bureaus under that structure. The Pesticide Laboratory is in charge of all pesticide programs; however, the disinfectant program is still located within the physical confines of the Food Laboratory because years ago, when I began the program in Florida, the decision was made not to duplicate an expensive microbiology section.

The state of Florida established its disinfectant testing program in 1968–69. I was asked to initiate the program and I spent one to two weeks in the U.S. Department of Agriculture laboratory in Beltsville, Maryland, under Dr. Ortenzio learning procedural techniques and interpretations. The Florida program (Table 3) has now tested over 3,000 samples of antimicrobials. The current program is divided into three areas (Table 4): 1) state enforcement; 2) Environmental Protection Agency (EPA) grant (in effect for the last three to four years); and 3) state purchasing—through the Department of General Services and School Plant Management Testing. I am pleased that ours was one of the earliest programs establishing requirements that products pass efficacy testing before purchases were awarded to low bidders in large state purchases; these early specifications are shown in Table 5.

So our experiences with the AOAC use dilution procedure, as well as other testing procedures, are

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Martha E. Rhodes, Ph.D., is chief of the Food Laboratory, Division of Chemistry, in the Florida Department of Agriculture and Consumer Services. She was the 1979 recipient of the American Society for Microbiology's P.R. Edwards Award for outstanding microbiologist for the southeastern branch. Dr. Rhodes is president of the Association of Food and Drug Officials, an international association of state, federal and territorial drug officials. She is editor of the book *Food Mycology* and was one of seven U.S. recipients of the Diamond Jubilee Award honoring the 75th anniversary of the Food and Drug Act

TABLE 1
Florida Department of Agriculture and Consumer Services

- Division of Administration
- Division of Consumer Services
- Division of Inspection
- Division of Chemistry
- Division of Forestry
- Division of Fruit and Vegetable Inspection
- Division of Plant Industry
- Division of Dairy Industry
- Division of Animal Industry
- Division of Standards
- Division of Marketing

- Food Laboratory
- Feed Laboratory
- Seed Laboratory
- Fertilizer Laboratory
- Pesticide Laboratory
- Chemical Residue Laboratory
- Commodity Testing Laboratory
- Methods Development Laboratory

Fiscal Year	No. of Samples	% Ineffective
68-69	8	25.0
69-70	201	32.8
70-71	347	30.0
71-72	265	21.9
72-73	118	28.8
73-74	201	21.9
74-75	173	18.5
75-76	157	9.6
76-77	136	13.2
77-78	153	16.3
78-79	140	17.9
79-80	106	18.9
80-81	202	18.8
81-82	289	24.2
Totals	2,496	22.1%

Type Samples	Fiscal '80-'81	Fiscal '81-'82	Fiscal '82-'83
State enforcement	63	109	
EPA enforcement	102	204	
State purchasing	17	18	
Company	—	—	
Totals	182	331	

TABLE 5
Early Specifications

Cleaner, Disinfectant and Deodorant Concentrate

Maximum use dilution 2 oz. per gallon of water and resulting solution shall be an effective cleaner, deodorant, and a germicide against the following organisms, as determined by AOAC 10th edition 5.001 through 5.011.

[illegible]

ATCC No. 6538 *Staphylococcus aureus*
ATCC No. 6539 *Salmonella typhosa*
ATCC No. 10708 *Salmonella choleraesuis*
ATCC No. 15442 *Pseudomonas aeruginosa*
ATCC No. 640 *Tricophyton interdigitale*

The product shall not contain iodines, arsenicals, mercury compounds, formaldehydes, free acid or abrasives. The in-use solution shall not cause skin irritation after continuous use. The product must be registered with the Florida Department of Agriculture and Consumer Services.

Product Type	Liquid		Spray	
	Samples	%	Samples	%
Quaternary Ammonium	71	22.5	19	21.1
Phenolic	58	20.7	12	0
Other	22	18.2	—	—

	Liquid		Spray	
Product	Samples	%	Samples	%
Quaternary Ammonium	141	37.6	28	7.1
Phenolic	105	27.6	23	4.3
Other	37	13.5	—	—

1981 through March 1983	
404	Products tested
7	Regulatory action indicated multiple lots ineffective
1.7%	Of products tested

not of short duration, and we have not just suddenly begun our activities in this area.

What are our current experiences with the procedure and what are current statistics? First of all, I think we all realize that statistics often show precisely what we wish them to show. For example, when we examined a computer search for a six-month period last year on a request for records, we found that only 12 percent of individual products failed test procedures. A company obtained a full year of records and its review indicated that 60 percent of quaternaries we tested had failed. This was not actually true, for they apparently did not identify composition in one-third of the samples.

If only the percent of ineffective samples is examined, this seems inordinately high, as indicated in Tables 6 and 7, which show that ineffective quaternary ammonium samples increased from 22.5 percent to 37.6 percent between 1980 and 1982. However, examining statistics based on samples is in error here for two reasons. First, sampling is not random, but rightly focuses on companies with previous violations or product categories frequently showing problems in effectiveness. Second, serum use as an organic load was not routinely used until this past year. All records on all products and companies have been pulled for calendar years 1981, 1982 and the first quarter of 1983, and a copy of this has been shared with your association.

Table 8 reveals that for this period of over two years, 404 individual products were tested. Only 7 of these are currently in the status of warranting some statewide regulatory action after having multiple lots tested revealing ineffectiveness against certain organisms. This number only represents 0.7 percent of the products tested.

Of the 404 products tested, 94—23 percent of the total—did have at least one failing test. However, Table 9 reveals that, overall, less than 20 percent of the products had any problems on testing. Three samples were tested with the wrong label. For two of them, the companies had actually registered a label in Florida that was more restrictive in claims than that on the product in the marketplace. At least two companies have verified our testing and changed their claims accordingly. Two have stopped making their products. Seven products had as their only violation a lack of proper registration.

More Serious Problem

Two hospital disinfectant-type products had a much more serious problem than any failure of a use dilution procedure in 1982-83. They were received with viable bacteria growing in them as shown in Table 10. One product had a very high count of gram positive rods. Investigation revealed that the company had mistakenly placed the disinfectant in a drum previously containing a s[illegible] tank additive.

The second contaminated disinfectant was received with 140,000/ml viable *Pseudomonas cepacia* growing in it. Table 11 shows that six lots of that particular product have been tested with all samples ineffective against *Pseudomonas*—most lots giving around 26 positive tubes out of 40. Only one sample was contaminated and subsequent subcultures of the five-gallon drum revealed three other isolates. This was a hospital type disinfectant, and Table 12 indicates the types of infections associated with the contaminant. Table 13 shows the many types of products from which this organism has been isolated within the past few years.

Tables 14 and 15 show current levels of testing activity in two other states—North Carolina and Virginia. In 1982, the North Carolina Department of Agriculture tested 423 samples involving 257 products of which 11 or 2.6 percent were ineffective: 10 against *Pseudomonas*; one of these 10 was also not fungicidal and one was ineffective against staphylococcus. Three other products have failed testing procedures during 1983.

> **"Operator variability is constantly present in any analytical procedure performed in any laboratory. This will always be a valid concern."**

The state of Virginia in 1982 tested 55 products, 10 of which were judged to be ineffective.

Table 16 indicates some shared testing between three state labs, including Florida. For the particular products involved, I also sent the two to a private laboratory which routinely does quality control for some CSMA member companies, and they obtained the same results.

Chief Regulatory Concern

Perhaps this would be a good opportunity to express another point concerning the states' programs. Our main regulatory concern is with those products which show repeated reproducible lack of effectiveness with either the use dilution procedure or the fungicidal procedure with multiple lots, an example of which is shown in the next two tables. Table 17 indicates individual lots tested. Table 18 indicates the positive carriers for each lot tested, i.e., on the first line 12/40 indicates 12 positive tubes out of 40 carriers. The closed circles indicate growth of *Trichophyton* after 5, 10 and 15 minutes' exposure. Each line is a different sample.

TABLE [illegible]

3	Wrong label registered or supplied to the laboratory.
1	
2	Changed claims.
1	Tested with serum in error.
1	For use only in rug shampoo—effective.
1	Wrong dilution used on one sample; subsequent samples effective.
2	Company stopped making products.
7	Only violation was lack of registration.
2	Adulterated with viable organisms.
	Conclusion: less than 20% ineffective

1. Gram positive rods TNTC
   Product placed in drum in which septic tank treatment product (live culture) had been previously

2. Gram negative rods
   140,000/ml
   Blue fluorescent pigment
   Pseudomonas aeruginosa or P. cepacia

Nitrate
Glucose
Decarboxylase
Oxidase
Lysine decarboxylase
Indole
Urease
Inositol
Mannitol
Adonitol
Rhamnose-sucrose
Ornithine decarboxylase
Voges-Proskauer
Citrate
Malonate
Tryptophane deaminase
Esculin
Gelatin liquefaction
Hydrogen sulfide
Maltose
Arabinose
Sorbitol

Six lots found ineffective against *Pseudomonas* 26/40
Subsequent analysis 5-gal can yielded gram positive cocci. *P. cepacia* original isolate. Additional gram negative rods

Meningitis
Septicemia
Necrotizing pneumonitis
Pneumonia
Septic arthritis
Chronic granulomatous disease
Postoperative wound infections
Cystic fibrosis
Endocarditis
Urinary tract infections
Abscesses
Conjunctivitis
Peritonitis

TABLE 13
Sources of Isolation of *Pseudomonas cepacia*

Decayed onions
Rotting tree trunks
Soil
Tap and distilled water
Aqueous/aquatic environs
Raw and pasteurized mil
Saline solution
Flower vases
Babies' thermometers
Anesthetics
Ultrasonic nebulizers
Incubators
Respirators
Humidifiers
Water baths
Pressure transducers
Intravenous cannulae
Intravenous catheters
Hemodialysis coils
Peritoneal dialysis machi
Anesthesia bottles
Intravenous infusions
Hand dips
Urinary catheter kits
Baby lotions
Normal human serum albumi
Aerosol polymyxin
Dimethylbenzylammonium chloride
Phenoxypolyethoxyethanol
Chlorhexidine
Cetrimide
Hexachlorophene
Povidone-iodine
Lidocaine
Propamidine
Ploloxidiene
Methylprednisolone
Cryoprecipitates

Source: Gilardi, *Lab Management*, 1983.

1982	423	Samples
	257	Products
	11	Ineffective products (2.6%)
		10 *Pseudomonas*
		1 Fungicidal
		1 Staphylococcus
1983	3	Additional products ineffective

1982	55 Products tested
	10 Failed AOAC procedures

	Florida	North Carolina	Virginia	EPA
Product A				
Serum and hard water	17/20	9/60	8/60	
	34/40	15/60	2/10	w/o serum
Product B				
w/o serum	8/40	15/60	24/60	failed
	8/60	17/60	26/60	
	13/20	11/60	30/60	

Company Z	Product A	13	Code lots tested
		13	Found ineffective against both *Pseudomonas* and *Trichophyton*
	Product B	10	Code lots tested
		10	Ineffective against *Pseudomonas* and *Trichophyton*
	Product C	7	Lots: 5 ineffective
	Product D	5	Lots: 3 ineffective
	Product E	3	Lots: All effective
	Product F	1	Lot: Effective

Company X							
Product X-1				Product X-2			
	Fungicidal				Fungicidal		
Pseud	5	10	15	*Pseud*	2	10	15
12/40	●	●	●	22/70	●	●	●
8/40	●	●	●	7/30	●	●	●
4/60	●	●	●	6/30	●	●	●
5/40	●	●	●	16/40	●	●	●
6/50	●	●	●	40/80	●	●	●
6/50	●	●	●	5/20	●	●	●
6/50	●	●	●	12/20	●	●	●
4/40	●	●	●	19/20	●	●	●
8/40	●	●	●	10/20	●	●	●
3/40	●	●	●	13/20	●	●	●
7/40	●	●	●	11/20	●	●	●
				32/40	●	●	●

	Organism × 10^{-4}
AOAC—Remove. Not shaken	25
EPA—Shaken	12
Shaken—hot wire in interior	7
Rolled	13

	Vol	Final Conc
EPA	0 023 ml	1 ppm
Company	0 136 ml	6 ppm

TABLE 2
Neutralization of Quaternary Ammonium Compound

Procedures	Transfer ml	Transfer Moles	Lecithin Moles	Excess Lecithin
Florida	0.023	2.8×10^{-5}	8.5×10^{-3}	302
Company	0.136	1.7×10^{-4}	8.5×10^{-3}	50

37° with dessicant stock culture 1.3×10^{8}	
20 min	1.8×10^{8}
30 min	2.2×10^{8}
45 min	1.8×10^{8}
60 min	1.6×10^{8}

Product	Lots	% Short wt	Variation (14–18 g)
1	A	18.3	9.8–16.9 g
	B	6.8	13.8–18.0
2	A	1.1	12.6–16.2
	B	21.3	10.5–15.6
	C	4.4	13.9–16.2
3	A	20.7	12.5–16.4

	With Serum			Without Serum		
Product	5	10	15	5	10	15 min
D	●	●	●	—	—	—
B	●	●	—	—	—	—
E	●	●	—	—	—	—
BP	●	●	●	—	—	—
Q	●	●	●	—	—	—
VQ	●	●	●	●	—	—
W	●	●	●	—	—	—
L	●	●	●	—	—	—
A	●	●	—	—	—	—

We are very aware, as are many CSMA members, of the multitude of factors affecting the use dilution testing procedure, and we have offered our laboratory repeatedly to be actively involved in any examination of the methods or collaborative studies. Let's examine some of the factors affecting the procedures and some of our observations.

For ring carriers, one CSMA member had one of our rings examined metallurgically and found that it had a defect capable of hiding a *Pseudomonas* cell within the crevice. Yet our positive rings have been segregated over the past few months and all give negative results with subsequent testing with other products. No one disputes that reproducible quality with rings is extremely difficult to achieve. I would offer that alternative carriers and technologies are available. Microorganisms as well as isolated enzymes can now be immobilized and fixed in almost a monolayer to plastic and glass. These newer techniques may be beneficial to newer testing methods. We have found some very distinct and reproducible effects in the way that ring carriers are treated within the procedure.

Table 19 shows an aspect involving both carriers and organisms. The way in which the rings are handled on removal from the bacterial culture significantly affects the numbers of organisms remaining on the ring. The AOAC procedure speaks merely to removing of the rings. It does not indicate that they are to be shaken in any manner. We were instructed by EPA to shake vigorously to remove excess culture. We noted that some companies used a hot wire in the interior of the ring, whereas other companies knocked the rings down and rolled them on filter paper. The numbers in Table 19 are the results of multiple carriers and are reproducible figures. A test against 7 million organisms is greatly different from one against 25 million.

Ring Removal and Media

Also, we have become quite concerned over the joint interactions of two other factors: ring removal and media. Over the last few months we have come to the conclusion that the letheen medium currently being used is not an adequate neutralizer of most of the disinfectants tested. We are not the first to note this. Dey and Engley, as well as other authors, have graphically pointed out the limitations of the neutralizing capacity of the subculture medium. Numerous companies have indicated to us that the secondary tubes always reveal more positive carriers than the primary ones. Our testing has confirmed the fact that, even with the most rigorous shaking to remove product excess, we still obtain more positive tubes when secondary tubes are used. You do not suddenly regenerate the organisms; they are still viable—they just cannot grow. We have also demonstrated this quantitatively.

Table 20 indicates the different volume of carryover into the subculture medium when two different techniques are utilized: 1) a vigorous shaking as we were instructed by EPA, and 2) a company technique of careful removal without any shaking. When Quismo published his findings on this neutralization medium in the late 1940's it was felt that the lecithin content was perhaps neutralizing the quaternary ammonium compound on a mole-for-mole basis. Table 21 is a brief summary of some data which show that this is not true. When we removed as much product as possible from the rings, and the precise volume and millimoles of product being transferred were calculated, we theoretically still had a tremendous residual neutralizer present. Duplication of observed company technique transferred six times as great a quantity of quaternary into the subculture medium. Even though neutralization should have been very adequate in our case, secondary tubes still gave a greater number of positive carriers.

I will not discuss the variables of media further other than to state that our reading of the AOAC procedure indicates that the nutrient medium using the natural peptone is the one required and that is the medium which we utilize in our testing.

The current AOAC use dilution procedure indicates a drying time of 20 to 60 minutes. An initial study of this within our laboratory (Table 22) shows that there was no effect on the viability of the organism when it was dried for 20, 30, 45 or 60 minutes with or without dessicant. The results are not complete on the actual effects on the final results of the use dilution procedure.

Operator variability is constantly present in any analytical procedure performed in any laboratory. This will always be a valid concern. We attempt to address it by our procedure of not reporting analyses unless they are first confirmed by other analysts within the laboratory.

Short Weight

In addition to operator variability, we are concerned with product variability. Table 23 indicates the amount of variability within three dry products. Lots of individual products exhibited from 1 to 21 percent short weight. Some individual packets were as much as 30 percent short of product. In addition, three individual lots of quaternary were submitted to the Pesticide Laboratory for chemical analysis because one had been represented as containing 33 percent greater quaternary, yet had had identical

Continued on page 64

out the industry, by which old products can be compared and new ones developed.

Q What do you foresee will be the biggest single issue facing your industry in the coming year? And also, what, if anything, is your division planning to do about it?

A I would say the biggest single issue facing our industry is the changing maintenance habits of floor polish users. This has been demonstrated in a couple of ways: one, through the clean-and-shine type products being sold in the consumer market; and two, with the trend toward increasing use of spray buffing in the I/I market. In both instances, we plan to continue monitoring the lifestyle and maintenance needs of our customers. Of course, we can't ignore the trend to "no wax" floors and its impact on the industry. But, as I mentioned before, this issue has been, and will continue tc addressed in an effective and realistic way.

Q If you were asked to describe your industry as it stands today in one brief sentence, what would you say?

A I'd describe our industry as realistic and dynamic. We recognize the changing needs of our customers, understand our technological capability, and respond quickly with the appropriate product or service.

Q Finally, if you were asked to give one word that best reflects the mood of your industry today, what would that word be?

A "Forward-thinking." □

States' View of Disinfectant Tests

Continued from page 20

use dilution test results. All three samples contained the same chloride content.

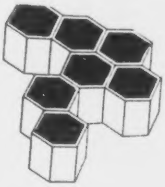
Another great variable contributing to many deficiencies is the claim of effectiveness in the presence of an organic soil load. In our laboratory, as well as in others, most products are just not fungicidal in the presence of serum, as seen in Table 24. All were effective without serum addition. This has been indicated by many others and if I may quote a letter to us:

> While attempting to confirm our fungicidal activity against *Trichophyton* we conducted an AOAC fungicide test on a quaternary compound. . . . The results of this test demonstrate that this compound would also not pass the AOAC test. Since it appears that there may be a number of products on the market which would not now pass the new AOAC fungicide test, you may want to survey other products to determine if they show acceptable fungicidal activity.

In conclusion, we see many different needs in disinfectant testing. First, however, let me state that we find the use dilution procedure acceptable, reproducible and useful data in judging product effectiveness. Because it is the procedure on which registration data is obtained, it must certainly be acceptable as a measure after the fact.

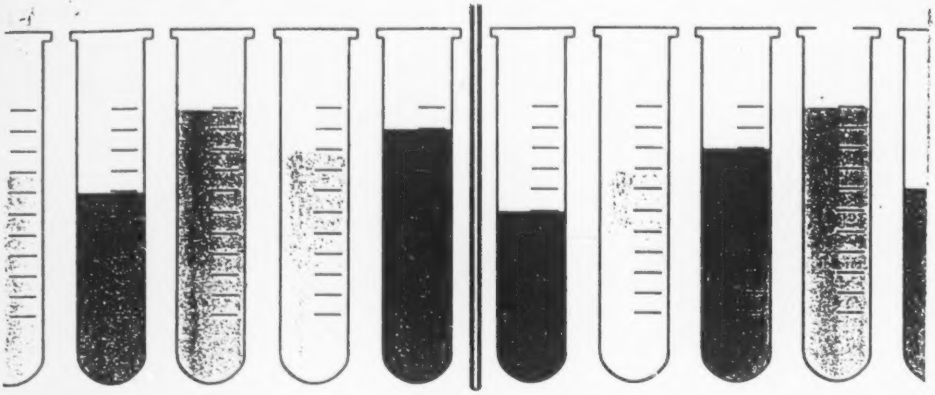
Recommendations

We certainly agree that use dilution conditions can be tightened. We feel that research and methods development for recovery of organisms in the user environment must be conducted. We would certainly hope that a standard chemical for testing could be established, giving predictable results. In addition, a check sample program involving all laboratories involved should be begun. We would wish that the EPA could permit the Beltsville laboratory to reopen for verification testing in instances involving conflicting results. We also feel a need to formulate a better neutralization medium and, until that time, to require secondary tube data on current registrations.



Florida again expresses its desire to participate fully and cooperatively with EPA, industry and private laboratories to resolve any methodology problems. We will continue our current testing program. The only alternative we have in our regulatory program is to notify those companies with repeated confirmed violations of our intent to suspend or deny registration within our state.

I look forward to working with many CSMA members in the future. The chemical specialties industry plays a very critical role in the health care of this nation, and I am sure that we are all equally concerned about our individual responsibilities in this area. □



DISINFECTANT TESTING

Measuring Product Performance

A Viewpoint From EPA

By Reto Engler
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About 30 years ago, government, industry and the scientific community, working together, developed a test to measure the performance of disinfectant products, known as the Association of Official Analytical Chemists (AOAC) Use Dilution Test. It has become the standard by which EPA and the states register disinfectant products. It is also widely used in enforcement to ensure the quality of disinfectants sold in the U.S. During the past year or more, however, the test has undergone close review and reevaluation because of poor reproducibility. Two different labs testing the same product using AOAC test procedures can often obtain different results. At the CSMA Mid-Year Meeting in May 1983, the Disinfectants and Sanitizers Division discussed the method—as well as other disinfectant test protocols—in a program entitled "Measuring Product Performance: Are Current Tests Adequate?" The following articles by Dr. Reto Engler and Dr. Martha Rhodes are adapted from the program.

I would like to state at the outset of this presentation that we at EPA never see any negative data on any of the disinfectants submitted to us for registration. All the data we are getting for registration are tests showing that the product

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passed the AOAC requirements. Therefore, I feel somewhat at a loss in that I cannot present a number of failing products versus passing ones.[*]

I think this brings us to at least one part of the real, deep-down problem of the AOAC test: that certain products seem to pass sometimes and to fail at other times. We are not in a position to say what this actually means. In many ways we at EPA may have contributed to perpetuating the situation because we, for obvious reasons, require passing tests. The reason is that the AOAC use dilution test is not a quantitative approach to testing the performance of disinfectants, and we do not have the information that would allow us to register or pass a product with a certain margin of safety or margin of confidence, even if we see some organisms growing under some test conditions. I think this is where we have to focus our attention.

Another statement which I would like to make right up front is that we are not saying that the AOAC test is useless or unreliable. Some such statements have been attributed to me. This is not true. I think it is a very useful test and has been used with success for years. What I believe is that we are now at a possible turning point where, based on experience and scientific knowledge, we can try to come up with a better test—one which can be better interpreted in a quantitative sense.

Along those lines, it is important that we also look at the past, because from a regulatory point of view we cannot come up with a brand new methodology, a brand new test tomorrow, and declare invalid everything we have done in the last 20 to 30 years. Whatever new approach we are going to choose has to be carefully crafted into the previous approaches to testing disinfectants, and improved methods have to be consistent with the older ones.

Important Development

There is one important development that I would like to mention. By way of an example I would like to focus on another test of the AOAC methods, which in a sense has experienced quite similar problems, although on a less broad base, primarily because there are fewer products involved: namely, the tubercucidal test.

Over the last three or four years we have essentially thrown up our hands at the tubercucidal testing because in a very similar fashion, the tests which were performed—sometimes in enforcement cases at Beltsville[†] and sometimes in independent testing laboratories—did not support the product's efficacy against *Bacillus tuberculosis*. The test also has a pass-fail outcome: everyone has searched for inconsistencies and "loopholes" in the test; and essentially the same problems have surfaced with it.

The associate referee has tried to do all kinds of little variations on the test: the media, the growth of the organism, for example, and he has not come up with any solution or answer; i.e., even after studying and changing several of the test parameters, sometimes the test worked and sometimes it didn't. The test did not lend itself to determine whether changing the parameters and "improving" the test was actually affecting the overall outcome.

Therefore, the associate referee had given up on the frustrating exercise of changing parameters because he could not determine whether any of the changes or improvements were actually providing a more reliable test.

The solution was obvious: he had to go to a quantitative measurement of product performance in order to determine which test parameters are, in fact, crucial for killing the organisms. The work is progressing well.

Viable Research Tool

In this particular case, the associate referee has chosen a kill curve, a time/kill curve of the organisms, to determine product performance. The initial studies indicate that the problems are essentially solved. He can now determine how many organisms are killed by a product, after a certain time and at a certain temperature. We now also have a good understanding that it was not the fault of test inconsistencies that gave us the picture of an "unreliable" test.

In other words, we now have a viable research tool in our hands which lets us change parameters such as concentration of organisms, time of contact and temperature of the reaction. And we can determine whether the changing of these parameters does, in fact, affect the killing curve.

I think we have learned a very useful lesson from that effort, and I would propose that we apply it to the use dilution test. Aside from "revising" or "improving" the test, we have to find the means to determine whether any or all of these revisions actually affect the test's reliability. We can do that only if we have quantitative test results for comparison.

For example, one of the papers presented in the CSMA program noted apparent fluctuations or differences between different sera. Some of these fluctuations may indicate a trend, at best, but I presume they would not hold up under rigorous statistical analysis.

EPA Fact Sheet

Because of the discussions on the AOAC use dilution test in the recent past, we have prepared a fact sheet on EPA's official position on the test. What we propose in that fact sheet is that we first look at the test as it exists today. We are currently examining it to figure out whether there are some parts which can—by mutual consensus between EPA, industry and the scientific community—be tightened down to make everybody perform the test in exactly the same fashion.

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[*] Dr. Engler is referring to Dr. Rhodes' article on p. 15.

[†] The U.S. Department of Agriculture laboratory in Beltsville, Maryland.

"We are planning to incorporate the microbiological testing—because of its importance in health-related situations—into our laboratory audit program."

After we have done that, we have to look for a collaborative study on the reliability of the test—but here I would like to emphasize that it will be difficult to determine whether or not we have an ideal and absolutely perfect test when we test one of the disinfectant products which never fails and give it to six different laboratories, for example. We know what the outcome is going to be: the outcome is going to be that all six laboratories are capable of performing the test, we will get 0 out of 60 positive carriers, and we will presume that the test is absolutely reliable and reproducible.

In other words, if we test some very strong disinfectant product in the collaborative study, we may fool ourselves and conclude that the test is actually reproducible every time we do it when, in fact, small variances in the test may have been overcome by the powerful disinfectant chemical.

Therefore, I believe that before we embark on a long and costly collaborative study, we have to think about the quantitative interpretation of our testing procedures, and address the outcome of the test at its limit of performance, i.e., the limit between passing and failing.

Once that is completed, I think we will have a test that we all can rely on. Any test procedure we devise will have to have confidence limits, which will provide us with limits of certainty that a product works, whether for the purpose of registration or for the purpose of enforcement.

We have to get away from the line of black and white—1 out of 60 passes and 2 out of 60 don't pass. This is scientifically and statistically an untenable position. We need to know more about a product; we need to know that it has a high probability of disinfecting an object. We have to establish the standards for this probability with certain confidence intervals. Again, I believe that once this is achieved we can make much more educated and correct decisions, whether for registering a product or for taking enforcement actions against a product.

The last point I would like to mention relates to the laboratory procedures, recordkeeping of scientific results, and reporting of tests.

We are planning to incorporate the microbiological testing—because of its importance in health-related situations—into our laboratory audit program. I think that this will help us to understand more about testing, testing procedures, and quality of testing.

It will also strengthen our dialogue and our interaction with the sector of the chemical industry that is performing these tests, and with the sector of the industry that is relying on the tests, either in their own laboratories or in contract testing laboratories.

In summary, the AOAC use dilution test is a good test for gathering at least presumptive evidence that a product will kill microorganisms on inanimate objects. The test's shortcomings may be, in part, procedural, but the major difficulty lies with the quantitative interpretation of test results. The test has not been changed or adapted in over 20 years.

We propose now to reevaluate the procedural aspects, but, more important, to apply the powerful statistical evaluation process to the AOAC use dilution test. I believe that this latter issue contributes most significantly to the antiquation of the test—in a scientific world where we have learned that the *significance* of differences is sometimes more crucial than differences, or apparent differences. ☐

* * *

Nosocomial Infection Surveillance, 1984

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Introduction

Nosocomial infections cause substantial morbidity and mortality, prolong the hospital stay of affected patients, and increase direct patient-care costs (*1-5*). Since 1970, the National Nosocomial Infections Surveillance System (NNIS) has collected and analyzed data on the frequency of nosocomial infections in U.S. hospitals. This report provides descriptive data on nosocomial infections in a sample of U.S. hospitals in 1984.

Materials and Methods

The methods used in this surveillance system and the characteristics of participating hospitals have been described in detail (*4,6*). In brief, hospitals participating in NNIS conduct active hospital-wide surveillance using uniform definitions of nosocomial infections. Although the definitions are specific for different sites of infection, onset must occur during hospitalization or shortly after discharge, and the infection may not be present or incubating at the time of the patient's admission. Each month data are recorded on standardized forms that are sent to CDC, where they are coded, edited, and entered into a computer before being analyzed. In 1984, 51 hospitals regularly (≥ 9 months) reported data to CDC. For each nosocomial infection detected, the following information was reported: site of infection; date of onset; hospital service on which the patient was placed; age and sex of the patient; pathogens isolated; occurrence of secondary bacteremia; antimicrobial susceptibility of bacterial pathogens; and, for those patients who died with a nosocomial infection, the relationship of the infection to death. In addition, the hospitals reported the number of patients discharged each month from six primary services: medicine, surgery, obstetrics, gynecology, pediatrics, and newborn.

Results

The NNIS Sample. The hospitals participating in NNIS are not a probability sample of U.S. hospitals; however, those hospitals that regularly reported data in 1984 ranged in size from 80 to 1,200 beds, were located throughout the United States, and were owned by state and local governments, as well as by profit and nonprofit organizations. The geographic distribution of the 51 hospitals among the four regions of the country (Northeast, North Central, South, and West) was roughly the same as that for all 6,375 U.S. acute-care hospitals included in the American Hospital Association Annual Survey of Hospitals (*7*). Hospitals affiliated with medical schools, referred to as teaching hospitals, are still greatly overrepresented among the NNIS hospitals; 61% (31/51) of the NNIS hospitals are teaching hospitals, whereas only 17% of the hospitals across the country are affiliated with a medical school. Similarly, the 51 NNIS hospitals tend to be large, with a median size of 406 beds, compared with a median size of only 112 beds for the 6,375 U.S. acute-care hospitals (*7*).

Despite these limitations, previous analyses have shown that data collected in NNIS can be usefully interpreted by stratifying the 51 reporting hospitals into three groups: 1) 20 (39%) nonteaching hospitals, 2) 18 (35%) small teaching hospitals of 500 or fewer beds, and 3) 13 (26%) large teaching hospitals of more than 500 beds (*4,6*).

The overall infection rate (number of hospital-acquired infections per 1,000 patients discharged) was highest in the large teaching hospitals and lowest in the nonteaching hospitals (Table 1). In all three hospital categories, the infection rate was highest on the surgery service, followed by the medicine and gynecology services (Table 2). On each of the six primary services, the infection rate was highest at the large teaching hospitals and lowest at the nonteaching hospitals, with the exception of the gynecology service rate, which was highest at small teaching hospitals.

In all three hospital categories, the urinary tract was the site most frequently infected, followed by lower respiratory tract or surgical wound infections (Table 3). For each site of infection, the infection rates were highest in the large teaching hospitals and lowest in the nonteaching hospitals.

Infections of the urinary tract, of surgical wounds, and of the lower respiratory tract accounted for almost three-fourths of the infections in all three hospital categories (Table 4). Primary bacteremia and cutaneous infections accounted for a higher percentage of infections in the large teaching hospitals than in the other hospitals.

Combined Rates by Service and Site. In general, the site-specific infection rate on each service was highest in the large teaching hospitals and lowest in the nonteaching hospitals

TABLE 1. Infection rates (cases/1,000 discharges), by hospital category, 1984

Hospital category	Infections	Discharges	Rate
Nonteaching	4,960	223,909	22.2
Small teaching	9,031	267,078	33.8
Large teaching	12,974	313,697	41.4
Total	**26,965**	**804,684**	**33.5**

TABLE 2. Infection rates (cases/1,000 discharges), by hospital category and service, 1984

	Service*					
Hospital category	**SURG**	**MED**	**GYN**	**OB**	**NEW**	**PED**
Nonteaching	30.8	23.3	8.6	5.6	6.6	1.2
Small teaching	47.3	38.1	35.2	14.9	14.7	14.6
Large teaching	59.3	46.9	31.7	20.3	17.3	16.6
Total	**46.7**	**36.5**	**28.1**	**15.3**	**14.4**	**13.3**

*SURG = surgery, MED = medicine, GYN = gynecology, OB = obstetrics, NEW = newborn, PED = pediatrics

(Table 5). In each hospital category, urinary tract infections occurred predominantly on the medicine, surgery, and gynecology services. Surgical wound infections occurred primarily on the surgery, gynecology, and obstetrics services. Lower respiratory infections occurred predominantly on the surgery and medicine services. Primary bacteremia occurred most frequently on the medicine and surgery services at nonteaching and large teaching hospitals. At small teaching hospitals, primary bacteremia was most frequently seen on the medicine and pediatrics services, followed by the newborn and surgery services. Cutaneous infections occurred primarily on the newborn service in each hospital category.

Pathogens. Of the 26,965 infections reported, 64% were caused by single pathogens, and 20% were caused by multiple pathogens (Figure 1). No pathogen was identified in 6% of the infections, and no culture was obtained in 10%. Of the 84% of infections in which a pathogen was identified, 86% were caused by aerobic bacteria, 2% by anaerobic bacteria, and 8% by fungi. Viruses, protozoa, and parasites collectively accounted for 5% of the infections of known etiology.

Escherichia coli, Pseudomonas aeruginosa, enterococci, and *Staphylococcus aureus* were the most frequently reported pathogens (Table 6). *E. coli* was the pathogen most often reported on all services except pediatrics and newborn, where *S. aureus* was the most common. *P. aeruginosa* was the second most frequently identified pathogen on the medicine and surgery services, whereas enterococci were second on the gynecology and obstetrics services. Coagulase-negative staphylococci were the second most frequently identified pathogens on the pediatrics and newborn services.

TABLE 3. Infection rates (cases/1,000 discharges), by hospital category and site of infection, 1984

	Site*					
Hospital category	UTI	SWI	LRI	BACT	CUT	Other
Nonteaching	9.9	3.6	4.2	1.3	1.1	2.0
Small teaching	13.9	6.0	5.4	1.9	1.8	4.7
Large teaching	14.2	6.6	7.7	3.9	2.6	6.4
Total	**12.9**	**5.6**	**6.0**	**2.5**	**1.9**	**4.6**

*UTI = urinary tract infection, SWI = surgical wound infection, LRI = lower respiratory infection, BACT = primary bacteremia, CUT = cutaneous infection

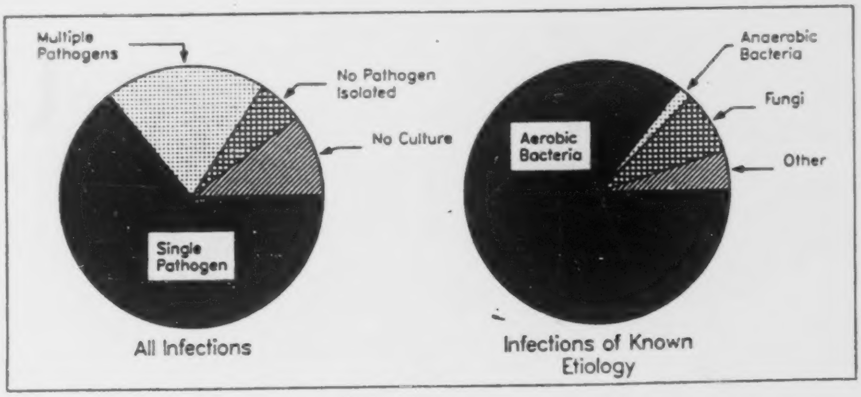
TABLE 4. Percentage distribution of infections at each of the major sites, by hospital category, 1984

	Hospital category			
Site	**Nonteaching**	**Small teaching**	**Large teaching**	**Total**
UTI	44.6	41.2	34.2	**38.5**
SWI	16.0	17.8	16.0	**16.6**
LRI	19.2	15.9	18.6	**17.8**
BACT	6.0	5.7	9.4	**7.5**
CUT	4.9	5.4	6.3	**5.8**
Other	9.3	14.0	15.4	**13.8**

TABLE 5. Site-specific infection rates (cases/1,000 discharges), by service, 1984

	Site						
Service	**UTI**	**SWI**	**LRI**	**BACT**	**CUT**	**Other**	**All sites**
1. Nonteaching hospitals							
SURG	12.1	8.5	5.4	1.3	1.4	2.0	30.8
MED	12.6	0.4	5.2	1.9	0.8	2.3	23.3
GYN	5.8	1.6	0.1	0.1	0.1	0.8	8.6
OB	1.1	2.4	0.1	0.1	0.5	1.4	5.6
PED	0.0	0.1	0.1	0.0	0.1	0.9	1.2
NEW	0.5	0.2	1.8	0.6	2.6	2.9	8.6
Total	**9.9**	**3.6**	**4.2**	**1.3**	**1.1**	2.0	**22.2**
2. Small teaching hospitals							
SURG	17.7	13.6	7.8	1.8	1.6	4.7	47.3
MED	20.1	0.6	7.5	2.8	1.7	5.3	38.1
GYN	19.9	11.1	1.3	0.4	0.2	2.2	35.2
OB	3.8	6.8	0.3	0.2	0.5	3.4	14.9
PED	2.0	0.6	2.0	2.4	2.3	5.2	14.6
NEW	0.6	0.2	1.4	2.0	4.8	5.6	14.7
Total	**13.9**	**6.0**	**5.4**	**1.9**	**1.8**	4.7	**33.8**
3. Large teaching hospitals							
SURG	19.5	15.0	11.2	4.2	3.3	6.1	59.3
MED	19.5	1.2	10.2	5.7	3.0	7.3	46.9
GYN	14.4	10.2	2.6	0.9	0.6	3.1	31.7
OB	4.2	6.6	0.5	0.9	0.5	7.5	20.3
PED	2.8	1.6	3.9	2.1	1.2	4.9	16.6
NEW	1.0	0.3	2.9	3.6	3.7	5.6	17.4
Total	**14.2**	**6.6**	**7.7**	**3.9**	**2.6**	6.4	**41.4**

FIGURE 1. Distribution of infections, by etiology, 1984



E. coli was the pathogen most frequently associated with urinary tract infections, followed by enterococci and *P. aeruginosa* (Table 7). *S. aureus* was the pathogen most often associated with surgical wound infections, followed by enterococci and *E. coli*. *P. aeruginosa* was the pathogen most frequently associated with lower respiratory tract infections, followed by *S. aureus* and *Klebsiella* spp. Coagulase-negative staphylococci were the pathogens most commonly associated with primary bacteremia, followed by *S. aureus* and *E. coli*.

When the pathogens causing infections at the five major sites were examined by service, interesting differences were noted (Table 8). On all six services, *E. coli* was the pathogen most often isolated from the urinary tract. Enterococci were the second most frequently isolated pathogens from the urinary tract on the obstetrics, gynecology, and medicine services, whereas *P. aeruginosa* was the second most commonly isolated pathogen from the urinary tract on the surgery and pediatrics services, and *Klebsiella* spp. were second on the newborn service. *S. aureus* was the pathogen most often associated with surgical wound infections on all services except gynecology, where *E. coli* was isolated most frequently. The pathogen most frequently associated with lower respiratory infections on all services was *P. aeruginosa*, with *S. aureus* second on all but the gynecology and newborn services. Coagulase-negative staphylococci were most often associated with primary bacteremia on the pediatrics, newborn, and surgery services, whereas *S. aureus* was the pathogen most frequently associated with bacteremia on the medicine and obstetrics services. *E. coli* and *Bacteroides* spp. were isolated with the highest frequency in association with primary bactere-

TABLE 6. The 15 most frequently isolated pathogens and their percentage distribution on each service, 1984

	Service							
Pathogen	MED	SURG	OB	GYN	PED	NEW	Total isolates	%
E. coli	19.6	16.2	21.2	29.8	11.4	9.3	5,266	17.8
P. aeruginosa	11.4	13.0	1.3	4.3	9.7	6.7	3,366	11.4
Enterococci	9.6	10.5	16.6	18.1	5.3	5.7	3,083	10.4
S. aureus	9.2	10.4	8.0	5.8	16.6	24.8	3,059	10.3
Klebsiella spp.	9.0	6.9	2.1	4.8	6.6	6.7	2,193	7.4
Coagulase-negative staphylococci	5.6	6.1	5.7	5.2	13.2	15.3	1,868	6.3
Enterobacter spp.	4.7	7.5	2.1	3.7	4.2	3.7	1,748	5.9
Candida spp.	7.0	4.9	1.1	2.2	7.6	3.8	1,620	5.5
Proteus spp.	5.6	5.4	3.4	5.3	0.3	1.0	1,522	5.1
Serratia spp.	2.1	2.9	0.2	0.3	1.4	1.3	691	2.3
Other fungi	2.3	1.5	0.1	0.1	1.2	1.0	496	1.7
Citrobacter spp.	1.5	1.5	1.1	0.8	1.0	0.8	414	1.4
Bacteroides spp.	0.6	1.4	4.6	2.8	0.3	0.2	355	1.2
Group B *Streptococcus*	0.8	0.5	7.9	3.8	1.2	6.2	348	1.2
Other anaerobes	0.9	0.9	4.8	2.0	0.3	0.2	300	1.0
All others*	10.1	10.4	19.8	11.0	19.7	13.3	3,253	11.1
Number of Isolates	11,304	14,596	1,024	1,016	590	1,032	29,562	100.0

*No other pathogen accounted for more than 3% of the isolates on any service.

mia on the gynecology service. *S. aureus* was most commonly associated with cutaneous infections and was followed by coagulase-negative staphylococci on all services except surgery and obstetrics. On surgery, *S. aureus* was first, followed by *P. aeruginosa*; on obstetrics, *E. coli* was isolated most frequently, followed by *S. aureus*.

Secondary Bacteremia. Secondary bacteremia was defined as a bloodstream infection with an organism that was also isolated from an infection at another site. Secondary bacteremia was reported most frequently by large teaching hospitals and least frequently by nonteaching hospitals (Table 9). Secondary bacteremia occurred most often on the pediatrics service in teaching hospitals, followed by the medicine, newborn, and surgery services, and it occurred least frequently on the obstetrics and gynecology services. In nonteaching hospitals secondary bacteremia occurred most often on the medicine, obstetrics, and surgery services and least often on the newborn, gynecology, and pediatrics services. For all hospital categories, secondary bacteremia was associated less frequently with urinary tract, surgical wound lower respiratory tract, and cutaneous infections than with infections, collectively, at "other" sites (Table 10). With respect to the four major sites, and excluding primary bacteremia secondary bacteremia occurred most often following cutaneous infections. It occurred most frequently in all hospitals following infections with *Acinetobacter* spp., *Bacteroides* spp. *S. aureus*, *Serratia* spp., and coagulase-negative staphylococci (Table 11), but this varied greatly within each hospital category. For example, in nonteaching hospitals, *S. aureus* was the main pathogen that caused secondary bacteremia. In small teaching hospitals, the frequency of secondary bacteremia due to coagulase-negative staphylococci has nearly doubled

TABLE 7. The 15 most frequently isolated pathogens and their percentage distribution for each site of infection, 1984

	Site							
Pathogen	UTI	SWI	LRI	BACT	CUT	Other	Total Isolates	%
E. coli	30.7	11.5	6.4	10.1	7.0	7.4	5,266	17.8
P. aeruginosa	12.7	8.9	16.9	7.6	9.2	6.7	3,366	11.4
Enterococci	14.7	12.1	1.5	7.1	8.8	7.0	3,063	10.4
S. aureus	1.6	18.6	12.9	12.3	28.9	14.6	3,059	10.3
Klebsiella spp.	8.0	5.2	11.6	7.8	3.8	4.6	2,193	7.4
Coagulase-negative staphylococci	3.4	8.3	1.5	14.9	11.5	11.6	1,868	6.3
Enterobacter spp.	4.8	7.0	9.4	6.3	4.5	3.9	1,748	5.9
Candida spp.	5.4	1.7	4.0	5.6	5.8	14.1	1,620	5.5
Proteus spp.	7.4	5.2	4.2	0.8	3.3	2.1	1,522	5.1
Serratia spp.	1.2	2.1	5.8	3.0	2.2	1.5	691	2.3
Other fungi	2.2	0.4	1.4	1.3	0.9	2.8	496	1.7
Citrobacter spp.	1.8	1.4	1.4	0.7	0.7	0.9	414	1.4
Bacteroides spp.	0.0	3.7	0.2	3.4	1.2	1.4	355	1.2
Group B *Streptococcus*	0.9	1.3	0.7	2.3	1.1	1.9	348	1.2
Other anaerobes	0.0	1.7	0.1	1.8	0.8	4.4	300	1.0
All others*	5.2	10.9	22.0	15.0	10.3	15.1	3,253	11.1
Number of Isolates	12,218	5,500	4,567	2,264	1,690	3,323	29,562	100.0

*No other pathogen accounted for more than 3% of the isolates at any site.

TABLE 8. Five most common pathogens isolated and percentage of total within each site and service, 1984

	Site									
	UTI		SWI		LRI		BACT		CUT	
Service	Pathogen	%	Pathogen	%	Pathogen	%	Pathogen	%	Pathogen	%
Medicine	*E. coli*	30.6	*S. aureus*	19.7	*P. aeruginosa*	16.6	*S. aureus*	14.4	*S. aureus*	26.3
	Enterococci	14.2	Enterococci	12.1	*S. aureus*	14.8	Coag-neg *staph.*	13.8	Coag-neg *staph.*	11.8
	P. aeruginosa	11.3	*P. aeruginosa*	9.3	*Klebsiella* spp.	12.2	*E. coli*	12.2	*P. aeruginosa*	11.0
	Klebsiella spp.	9.4	Coag-neg *staph.*	9.0	*Enterobacter* spp.	7.7	*P. aeruginosa*	9.2	Enterococci	9.1
	Proteus spp.	8.1	*E. coli*	6.9	*E. coli*	7.3	*Klebsiella* spp.	8.5	*Candida* spp.	6.6
Surgery	*E. coli*	29.2	*S. aureus*	19.0	*P. aeruginosa*	16.5	Coag-neg *staph.*	14.0	*S. aureus*	19.0
	P. aeruginosa	16.1	Enterococci	12.1	*S. aureus*	11.5	*S. aureus*	10.2	*P. aeruginosa*	12.9
	Enterococci	13.4	*E. coli*	11.5	*Enterobacter* spp.	11.4	*Enterobacter* spp.	9.2	Enterococci	10.7
	Proteus spp.	7.4	*P. aeruginosa*	9.7	*Klebsiella* spp.	11.2	Enterococci	9.1	Coag-neg *staph.*	10.1
	Klebsiella spp.	6.7	Coag-neg *staph.*	7.9	*Serratia* spp.	6.9	*Klebsiella* spp.	7.5	*E. coli*	7.9
Gynecology	*E. coli*	40.7	*E. coli*	15.1	*P. aeruginosa*	15.6	*E. coli*	16.0	*S. aureus*	18.8
	Enterococci	23.5	*S. aureus*	12.9	*Enterobacter* spp.	9.4	*Bacteroides* spp.	16.0	Coag-neg *staph.*	12.5
	Klebsiella spp.	6.7	Enterococci	12.9	*S. aureus*	6.3	Coag-neg *staph.*	8.0	*Morganella* spp.	12.5
	Proteus spp.	5.0	Coag-neg *staph.*	11.5	*Candida* spp.	6.3	*S. aureus*	8.0	Viruses	12.5
	P. aeruginosa	4.5	*Bacteroides* spp.	6.8	*Klebsiella* spp.	3.1	*Klebsiella* spp.	4.0	Other anaerobes	12.5
Obstetrics	*E. coli*	36.3	*S. aureus*	13.7	*P. aeruginosa*	7.7	*S. aureus*	14.3	*E. coli*	25.6
	Enterococci	28.8	*E. coli*	13.7	*S. aureus*	7.7	Other anaerobes	12.2	*S. aureus*	23.1
	Group B *strep.*	6.0	Enterococci	12.5	*Klebsiella* spp.	7.7	*E. coli*	8.2	Enterococci	10.3
	Coag-neg *staph.*	3.6	Coag-neg *staph.*	9.6	*E. coli*	7.7	Coag-neg *staph.*	6.1	Coag-neg *staph.*	7.7
	Proteus spp.	3.3	*Bacteroides* spp.	8.3	*Candida* spp.	7.7	Enterococci	6.1	Group B. *strep.*	5.1
Pediatrics	*E. coli*	30.4	*S. aureus*	34.8	*P. aeruginosa*	19.8	Coag-neg *staph.*	29.0	*S. aureus*	40.3
	P. aeruginosa	13.4	*E. coli*	10.6	*S. aureus*	11.6	*S. aureus*	14.0	Coag-neg *staph.*	19.4
	Enterococci	10.7	*P. aeruginosa*	10.6	*Klebsiella* spp	9.3	*E. coli*	10.8	*E. coli*	10.4
	Klebsiella spp.	10.7	Coag-neg *staph.*	10.6	*Enterobacter* spp.	7.0	*Klebsiella* spp.	6.5	*Candida* spp.	7.5
	Candida spp.	10.7	Enterococci	7.6	*Candida* spp.	3.5	*Candida* spp.	6.5	Enterococci	4.5
Newborn	*E. coli*	35.2	*S. aureus*	23.1	*P. aeruginosa*	29.5	Coag-neg *staph.*	20.8	*S. aureus*	54.5
	Klebsiella spp.	15.5	Coag-neg *staph.*	23.1	*Klebsiella* spp.	15.2	Group B. *strep.*	15.3	Coag-neg *staph.*	12.6
	Coag-neg *staph.*	9.9	*P. aeruginosa*	15.4	Coag-neg *staph.*	9.8	Enterococci	9.9	*E. coli*	6.1
	Enterococci	8.5	Enterococci	7.7	*E. coli*	8.0	*E. coli*	9.4	Enterococci	4.8
	Candida spp.	8.5	*Klebsiella* spp.	7.7	*S. aureus*	7.1	*Klebsiella* spp.	8.4	*Enterobacter* spp.	4.2

since 1983 (*6*). In addition, *Bacteroides* spp., *S. aureus*, Group B *Streptococcus*, and *Acinetobacter* were frequently associated with secondary bacteremia in small teaching hospitals. In large teaching hospitals, no pathogen predominated as the causative agent of secondary bacteremia.

TABLE 9. Percentage of infections* with secondary bacteremia, by service and hospital category, 1984

	Service						
Hospital category	**SURG**	**MED**	**GYN**	**OB**	**NEW**	**PED**	**All services**
Nonteaching	3.6	4.3	1.6	4.0	2.9	0.0	3.8
Small teaching	5.0	5.5	1.8	3.1	5.2	6.8	4.9
Large teaching	6.5	8.5	1.8	2.5	6.5	8.6	6.8
All hospitals	**5.4**	**6.6**	**1.8**	**2.8**	**5.5**	**7.8**	**5.6**

*Excluding primary bacteremia

TABLE 10. Percentage of infection with secondary bacteremia, by site* and hospital category, 1984

	Site					
Hospital category	**UTI**	**SWI**	**LRI**	**CUT**	**Other†**	**All sites**
Nonteaching	3.1	3.5	3.3	4.1	8.9	3.8
Small teaching	2.7	4.2	6.1	9.4	9.6	4.9
Large teaching	3.9	6.0	5.9	9.4	14.3	6.8
All hospitals	**3.3**	**4.9**	**5.4**	**8.6**	**12.0**	**5.6**

*Excluding primary bacteremia.

†Most frequently associated with cardiovascular (70.8%) and intra-abdominal infections (10.5%).

TABLE 11. Ten pathogens with the highest percentage of associated secondary bacteremia, by hospital category, 1984

	Nonteaching		Small teaching		Large teaching		All hospitals	
Pathogen	**No. of infections**	**% with secondary bacteremia**	**No. of infections**	**% with secondary bacteremia**	**No. of infections**	**% with secondary bacteremia**	**No. of infections**	**% with secondary bacteremia**
Acinetobacter spp.	21	0.0	30	10.0	85	22.4	136	16.2
Bacteroides spp	17	5.9	51	13.7	47	19.1	115	14.8
S. aureus	439	9.3	887	12.4	1,118	15.9	2,444	13.5
Serratia spp	99	6.1	118	5.9	239	18.0	456	12.3
Coagulase-negative staphylococci	151	3.3	449	11.1	529	13.4	1,129	11.2
Group B *Streptococcus*	35	2.9	87	10.3	79	10.1	201	9.0
Klebsiella spp.	290	4.8	475	4.6	667	10.6	1,432	7.5
Other fungi	34	5.9	139	2.9	180	10.0	353	6.8
Morganella spp	36	5.6	45	4.4	53	7.5	134	6.0
Other *Pseudomonas* spp	63	0.0	66	3.0	89	12.4	218	6.0

Antimicrobial Resistance. Resistance was defined as the number of resistant isolates divided by the number of organisms that were either sensitive or resistant, multiplied by 100. Methicillin-resistant *S. aureus* was most commonly reported from the large teaching hospitals (Table 12). In fact, for all the antimicrobials listed in Table 12, resistance was most often reported from the large teaching hospitals.

The percentages of *E. coli, Klebsiella pneumoniae, Serratia marcescens,* and *P. aeruginosa* organisms that were resistant to aminoglycosides and selected beta-lactam antibiotics varied according to the three hospital categories (Tables 13-16). Aminoglycoside resistance was most common in *P. aeruginosa* and *S. marcescens,* and cefotaxime or moxalactam resistance was most common in *P. aeruginosa.*

TABLE 12. Antimicrobial resistance of *Staphyloccocus aureus*, 1984

Hospital category	Number resistant (%)				
	Methicillin	Gentamicin	Clindamycin	Chloramphenicol	Erythromycin
Nonteaching	23 (6.0)	38 (8.6)	41 (9.1)	19 (5.4)	58 (11.9)
Small teaching	43 (4.6)	50 (5.9)	65 (7.2)	25 (3.0)	107 (10.9)
Large teaching	140 (11.3)	106 (10.6)	140 (10.4)	84 (7.2)	245 (18.0)

TABLE 13. Antimicrobial resistance of *Escherichia coli*, 1984

Hospital category	Number resistant (%)				
	Gentamicin	Tobramycin	Amikacin	Cefotaxime	Moxalactam
Nonteaching	28 (2.4)	11 (1.4)	9 (1.6)	1 (1.2)	0 (0.0)
Small teaching	48 (2.6)	19 (1.5)	11 (2.2)	6 (3.2)	9 (7.1)
Large teaching	46 (2.0)	51 (2.6)	21 (1.7)	9 (1.3)	3 (1.0)

TABLE 14. Antimicrobial resistance of *Klebsiella pneumoniae*, 1984

Hospital category	Number resistant (%)				
	Gentamicin	Tobramycin	Amikacin	Cefotaxime	Moxalactam
Nonteaching	20 (4.7)	12 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
Small teaching	26 (3.6)	12 (2.3)	7 (2.7)	6 (8.6)	5 (8.2)
Large teaching	67 (6.7)	47 (5.9)	24 (4.2)	5 (1.3)	7 (3.1)

TABLE 15. Antimicrobial resistance of *Serratia marcescens*, 1984

Hospital category	Number resistant (%)				
	Gentamicin	Tobramycin	Amikacin	Cefotaxime	Moxalactam
Nonteaching	10 (6.1)	11 (8.3)	6 (5.4)	3 (7.3)	0 (0.0)
Small teaching	13 (7.2)	16 (11.0)	3 (3.7)	4 (6.1)	6 (10.3)
Large teaching	41 (11.6)	52 (18.4)	18 (8.7)	21 (11.3)	8 (7.2)

Mortality. Data from individual hospitals are included in the mortality analyses if the hospital assessed and reported the relationship of infection to death for more than 50% of the infections in patients who died while hospitalized. The 42 hospitals that met this criterion reported a total of 22,432 infections; among the 1,253 patients who died, there were 1,811 infections for which the relationship of the infection to death was recorded. Approximately 1% of all nosocomial infections caused death, and 3% contributed to death (Table 17). Infections were more often reported to cause or contribute to death in small teaching and in nonteaching hospitals than in large teaching hospitals. Among infected patients who died while hospitalized, 9% of the infections reportedly caused death, 38% contributed to it, and 37% were not related to death; in 15% of these infections, the relationship of the infection to death could not be determined (Table 18).

TABLE 16. Antimicrobial resistance of *Pseudomonas aeruginosa*, 1984

Hospital category	Number resistant (%)									
	Gentamicin		Tobramycin		Amikacin		Cefotaxime		Moxalactam	
Nonteaching	111	(15.1)	43	(6.8)	23	(5.1)	74	(64.3)	30	(30.6)
Small teaching	91	(9.0)	40	(5.0)	33	(6.7)	163	(59.1)	137	(59.1)
Large teaching	228	(15.7)	117	(7.9)	54	(5.6)	180	(36.1)	121	(28.4)

TABLE 17. Percentage of infections reported as having caused or contributed to death of the patient, 1984

Hospital category	Number of infections	Percentage that caused death	Percentage that contributed to death
Nonteaching	3,553	0.7	3.9
Small teaching	8,609	1.1	3.1
Large teaching	10,270	0.5	2.8
Total	**22,432**	**0.7**	**3.1**

TABLE 18. Relationship of infection to death by hospital category, 1984*

Hospital category	Number (%)									
	Caused death		Contributed to death		Not related to death		Unknown		Total	
Nonteaching	23	(6.7)	139	(40.6)	138	(40.4)	42	(12.3)	342	(100)
Small teaching	96	(12.5)	268	(35.0)	251	(32.8)	151	(19.7)	766	(100)
Large teaching	47	(6.7)	287	(40.8)	288	(41.0)	81	(11.5)	703	(100)
Total	166	(9.2)	694	(38.3)	677	(37.4)	274	(15.1)	1,811	(100)

*There were 1,811 infections in 1,253 patients who died.

Discussion

Nosocomial infections remain an important cause of morbidity and mortality in U.S. hospitals. Data from NNIS, the only national source of prospectively collected data on hospital-acquired infections, show that the overall rate of nosocomial infections during 1984 was 3.4 infections per 100 patients discharged. This is similar to the infection rate reported for the 3-year period 1980-1982 (*4*) and for 1983 (*6*). By comparison, the Study on the Efficacy of Nosocomial Infection Control (SENIC) found that a nosocomial infection develops in 5%-6% of hospitalized patients (*8*). SENIC was a retrospective study involving a representative sample of U.S. hospitals in 1975-1976. NNIS data suggest that the true incidence of nosocomial infections is underestimated. Factors contributing to the underestimation include variability of the intensity of surveillance and availability of laboratory support, especially in diagnostic virology. Since identification of nosocomial viral infections depends on both laboratory detection and surveillance intensity, hospitals without virology laboratory support will be unlikely to detect most of these infections.

Since 1980 (*4*), nosocomial infection rates have been consistently highest in large teaching hospitals and lowest in nonteaching hospitals for all services and sites of infection, suggesting that the three-level stratification effectively defines hospital categories in which patients have different levels of risk for acquiring nosocomial infections. This difference in risk undoubtedly reflects severity of underlying illness (patient mix) and the extent to which invasive diagnostic and therapeutic procedures are performed in these hospitals.

As in 1980-1982 (*4*) and in 1983 (*6*), the infection rates were highest on the surgery and medicine services, probably because of their high-risk patient populations. The lowest infection rates were on the pediatrics and newborn services. One explanation for this lower rate may be that in NNIS hospitals, there are fewer high-risk children and newborns than adults, particularly in the small hospitals. Furthermore, most of the infants included in the newborn service are in well-baby nurseries, where the infection risk is expected to be lower. Another factor that may help explain the lower rates of infection on the pediatrics and newborn services is that only a small proportion of NNIS hospitals have diagnostic virology laboratories; therefore, many viral infections probably go undetected. Since children more often acquire nosocomial viral infections than adults (*9*), and since in one study viruses accounted for approximately 14% of nosocomial infections in children (*10*), NNIS hospitals are probably underreporting viral infections. In addition, other factors, such as the short time that many pediatric patients are hospitalized and the frequent use of isolation precautions on the pediatrics and newborn services, may reduce the incidence of nosocomial infections on these services.

In 1984, infection rates on different services and at different sites of infection within the three hospital categories varied little from those reported for 1983 (*6*). Since 1980-1982 (*4*), the primary bacteremia and lower respiratory tract infection rates have increased. The overall lower respiratory tract infection rate surpassed the rate of surgical wound infections in 1984. Whether this is an artifact of reporting or a true shift in the rates is not known.

Specimens for microbiologic testing were obtained from 90% of the patients reported to have a nosocomial infection. Aerobic bacteria were the most commonly identified etiologic agents. Anaerobic bacteria, fungi, parasites, and viruses were seldom reported, reflecting in part the frequency with which these pathogens are looked for, as well as the diagnostic laboratory capabilities of the hospitals.

E. coli was the most frequently identified pathogen on the four adult services, reflecting the fact that this organism was the primary cause of urinary tract infections on these services.

In contrast, *S. aureus* was the pathogen most often identified on the newborn and pediatric services. Coagulase-negative staphylococci were the second most frequent cause of nosocomial infections on the newborn and pediatrics services and were an important cause of bacteremia on all services except gynecology and obstetrics. Recent studies suggest that the increasing use of long-line catheters may be contributing to the emergence of coagulase negative staphylococci as an important cause of primary bacteremia (*11,12*).

Previous analyses of NNIS data have suggested that secondary bacteremia carries an increased risk of death (*13*). In all hospitals, the major sites of infection that were most likely to result in secondary bacteremia were cutaneous infections, followed by surgical wound and lower respiratory tract infections. Infections at sites other than the four major sites were, collectively, more frequently associated with secondary bacteremia. These include cardiovascular and intra-abdominal infections. An increase in cardiovascular surgery and in the use of long-line venous and arterial catheters may have accounted for the rise since 1983 in the percentage of infections associated with the cardiovascular system (*6*). Because of the increased risk of death associated with secondary bacteremia, these infections continue to be a high priority for prevention and control (*13*).

As in the past, the incidence of methicillin-resistant *S. aureus* (MRSA) infections was highest at large teaching hospitals (*4,6,14*), and between 1983 and 1984, these infections increased by more than 25% in each hospital category (*6*). Since 1983, the proportion of *S. aureus* organisms resistant to gentamicin and clindamycin increased at small teaching and at nonteaching hospitals, but at large teaching hospitals the proportion resistant to gentamicin decreased and that resistant to clindamycin remained about the same (*6*). The factors responsible for these resistance trends require further study. Recent work suggests that risk factors for MRSA may differ by type of hospital (*15*).

In 1984, compared with 1983, the proportion of *K. pneumoniae* organisms resistant to gentamicin and tobramycin decreased in large teaching hospitals and increased in nonteaching hospitals, however, resistance to amikacin increased in large teaching hospitals and decreased in both nonteaching and small teaching hospitals (*6*). Since 1982, the resistance of *P. aeruginosa* to both cefotaxime and moxalactam has increased in the small teaching hospitals, but the trend has been variable in nonteaching hospitals (*4,6*). Over the same period cefotaxime resistance has continued to decrease, and moxalactam resistance has been rising in the large teaching hospitals (*4,6*). Since the proportion of isolates tested against cefotaxime and moxalactam was small, these data should be interpreted with caution.

When compared with NNIS mortality data for 1980-1982 (*4*) and 1983 (*6*), the overall percentage of infections reported to cause or contribute to death in 1984 has not changed significantly. Since 1980, the large teaching hospitals have reported a slightly lower percentage of infections each year as causing or contributing to a patient's death (*4,6*). The small teaching hospitals reported about the same frequency, and the nonteaching hospitals reported a slight increase each year (*4,6*). Mortality data should be interpreted with caution, since standard criteria for assessing the relationship of infection to death do not exist.

This nationwide nosocomial surveillance system is expanding in four directions (*6*). First, microcomputer software called the Interactive Data Entry and Analysis System (IDEAS) has been developed to support nosocomial infection surveillance activities of NNIS hospitals. Beginning in October 1984, IDEAS was pilot tested in three hospitals and is now being used in 22 additional hospitals. This information management system not only helps to improve the quality and timeliness of nosocomial infection data collected in NNIS, but it also assists infection control practitioners in conducting more effective and efficient surveillance in their institutions. Second, additional hospitals are being added to the surveillance system so that the data obtained will be from a more representative sample of all acute-care hospitals in the United States. Since recruitment began in March 1985, 10 hospitals have been added and additional hospitals are being considered for enrollment. Third, in July 1985, the feasibility of collecting data on antimicrobial usage in NNIS hospitals was assessed. Hospitals with computerized pharmacy records wishing to participate in the study will report on the use of antimicrobial agents so that for selected nosocomial bacterial pathogens the relationship between usage and resistance can be evaluated. Fourth, strategies are being developed for determining a more sensitive indicator of patients' risk based on characteristics of both the patient and the hospital (such as the three size categories used in this report). When various levels of nosocomial infection risks can be calculated, infection rates among hospitals can be compared and the distribution of risks can be standardized; in addition, hospital-specific infection rates and secular trends can be evaluated more effectively.

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SPECTROSCOPY/SEPARATION METHODS

By Jay M. Ansell

THE SIGNIFICANCE OF RECENTLY REPORTED

Contamination of germicidal and nongermicidal agents

IN HYGIENIC HAND DISINFECTION

IT IS AN ESTABLISHED fact that the hands of health professionals are capable of transmitting infections from one patient to the next, and that the use of hygienic hand-wash disinfectants is a clinically significant approach to the control of the transmission of these infections. It is estimated that one-half of hospital-acquired infections might be avoided through prompt and adequate hand washing.[1] Recently, several cases of intrinsic microbial contamination of commercially available germicide solutions[2] have raised serious questions concerning the efficacy of these products as hand-washing agents.

The contamination of disinfectants with pathogens is of great concern. Florida's Department of Agriculture and Consumer Services routinely monitors selected disinfectants sold in the state. This program found 22.1% of the samples tested between 1968-1982 to be unacceptable.[3] Although this number reflects various measures of acceptability, including short weights, many products were found to be contaminated or ineffective against specific microorganisms. More recently, a benzalkonium chloride product was recalled because it was found to be contaminated with *Pseudomonas cepacia.*[4] Even soap bars were found to be reservoirs of microorganisms. Kabara summarizes studies showing 37 organisms including gram negative, gram positive organisms, anaerobes, and fungi isolated from bar soap.[5]

Detailed investigation into the one contamination incident concerning a povidone-iodine solution led Food and Drug Administration (FDA) compliance officials to conclude that the water deionizer may have been the growth medium and that the *Pseudomonas cepecia*-laden water was the source of contamination. Their conclusion resulted in an FDA letter sent to the pharmaceutical industry as an "informative reminder to properly validate and control deionized water systems," used in manufacturing which are "usually excellent breeding areas for microorganisms."

Germicidal agents must be handled with care. If proper precautions in manufacture or storage are not taken, these products may become contaminated. Indeed, even the liquid soaps recommended by Kabara have been associated with nosocomial infections through inadequate care of the dispenser.[6] It has been suggested that dispensers for liquid soap be disinfected before being refilled.[7] Care must be taken during all phases of manufacture, storage, and use to assure consistently effective hygienic hand disinfectants.

The relationship between these studies, the finding of microorganisms in products, and the transmittal of disease, is not clear.[5] Studies have failed to demonstrate the contamination of hands by such organisms following normal hand washing with contaminated soap bars.[7]

Iodophors and povidone-iodine, in particular, have found many hand-disinfection applications, and their efficacy has been supported in studies for many years. Peterson[8] cited 16 critical reviews on the antimicrobial use of povidone-iodine, which support broad spectrum antimicrobial activity. The Peterson report also discussed additional clinical studies representing more than 10,000 patients who, after topical treatment with povidone-iodine, showed reduced infections and increased healing.

In studies to judge the efficacy of germicidal hand-wash agents in hygienic hand disinfection, Sheena and Stiles[9,10] indicate that after testing a number of agents for short wash exposure time, only iodophor and chlorhexidine gluconate were notably better than the nongermicidal soap control. Sheena and Stiles conclude that soap and water are not adequate for general hand washing.

Most recently, the technique proposed for validation of hand washes in Germany[11] and Austria[12] was repeated by LaRocca, et al.[13] This confirmed, once again, the effectiveness of povidone-iodine in these uses.

Efforts to assure the manufacturing of acceptable products must be redoubled and attention brought to the potential for in-use contamination of these products. All the well-validated studies, however, show that, regardless of competitive claims, when manufactured, stored, and used in a suitable way, povidone-iodine is a broad-spectrum antimicrobial that is effective in topical

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Dr. Ansell is Manager, Regulatory Science, GAF Corporation.

therapy,[illegible] and that germicidal hand washes play an important role in the control of nosocomial infections.

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

December 4, 1985

Ms. Betsy B. Woodward
Chief, Food Laboratory
Division of Chemistry
Florida Dept. of Agriculture and Consumer Service
3125 Conner Blvd
Tallahassee, FL 32301

Dear Ms. Woodward,

Use-Dilution tests on the 5 disinfectant samples you shipped to us were done per your October 7, 1985 letter request. The samples, identified by numbers: 718, 866, 1861, 11765 and 6443, were tested against Pseudomonas aeruginosa with 5% v/v human serum as organic soil load, and in presence of hard water (400 ppm hardness). The results listed in order of testing are as follows:

FL Sample No.	Microbiology No.	Test Date	Results
1861	86-MB-01	11/13/85	31 pos. out of 60
6443	86-MB-02	11/14/85	28 pos. out of 60
11765	86-MB-03	11/15/85	19 pos. out of 60
866	86-MB-04	11/16/85	23 pos. out of 40
718	86-MB-05	11/22/85	15 pos. out of 40

In view of the rather unimpressive performance of the first three samples, samples 866 and 718 were subjected to 40-carrier rather than 60-carrier tests.

Heat inactivated GIBCO Human Serum (plasma-derived) was used as soil load in the first test (#1861).

In the remaining four tests, reconstituted Difco TC Human Serum (Dessicated) was used.

I trust this will serve your needs. Let me know if we can be of further assistance to you.

Sincerely,

T.J. Czerkowicz
Microbiologist
OPP/OPTS/BUD/SSB
(301) 344-2563/2187

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HOSPITAL INFECTION CONTROL

PRESENTING THE LATEST NEWS AND COMMENT IN THE FIELD OF HOSPITAL INFECTION CONTROL

VOLUME 14/NUMBER 3 (pages 29-44) MARCH 1986

Special report

Data lacking on safe, effective antiseptics and disinfectants

Think of the standard by which hospitals choose safe, effective antimicrobial agents as the needle.

Think of the evidence that those agents actually do what they are supposed to as the haystack.

Find the needle and you've solved one of the biggest dilemmas facing infection control practitioners today: How do hospitals choose safe and effective antiseptics and disinfectants?

According to the more than 20 ICPs, microbiologists, pharmacists, epidemiologists, and other experts interviewed for this report, there is no standard for hospital antimicrobial agents -- mostly because solid safety and efficacy data on many of those agents are sorely lacking.

Those data are lacking for two reasons, the experts say. First, the few independent, in-depth clinical studies that are performed on antimicrobial agents are not always readily available. Second, federal agencies apparently don't actually "regulate" antimicrobial agents -- nor do they provide accurate, up-to-date information on the safety and efficacy of those agents.

The U.S. Environmental Protection Agency registers hospital disinfectants in the registration division under the Office of Pesticides. When that division receives a question concerning the safety or efficacy of a specific product, the agency will only divulge whether the product is EPA-registered. (See related story, p. 36.) The data used by the EPA to approve a product for registration are submitted entirely by manufacturers, not by an independent panel or organization. In addition, once a product is registered, only in certain instances does the EPA enforce a disinfectant's label claims.

The U.S. Food and Drug Administration evaluated topical antimicrobials almost

Special report focuses on disinfectants, antiseptics

This issue of HIC includes the first part of a special report on hospital antimicrobial agents.

The report, which begins on this page and continues on page 37, features interviews with leading infection control experts about the difficulty in choosing hospital disinfectants and antiseptics. Next month, in the second half of this report, HIC will feature more expert advice on the safety and efficacy of specific antimicrobials.

Highlights of this issue:

- What FDA has available on antiseptics 33
- How EPA regulates disinfectants 36
- Testing employees for tuberculosis 37

a decade ago through its Advisory Review Panel on Over-the-Counter (OTC) Antimicrobial Products. That panel categorized the active ingredients in health care personnel handwashes and other topical antimicrobials in the 1970s.

However, many experts agreed that the FDA categorizations -- which were last published in 1978 -- are incomplete and outdated. The FDA will publish results of the most recent evaluations (which have taken place since 1978) in the panel's "final monograph." That monograph will permanently categorize specific active ingredients used in antimicrobial agents as either safe and effective or not. However, the final monograph "may not be ready until the year 2020, for all I know," according to one FDA spokesman, who declined to be identified.

The agency refuses to release any information regarding the panel's findings before the final monograph is published, according to another FDA spokesman in the Drug Evaluation Division, Office of Drug Standards. (See related story, page 33.)

As a result, some ICPs say they don't know where to turn for documented, solid information on antimicrobial agents.

"The Centers for Disease Control can't even make generic recommendations for hospital disinfectants anymore," said **ELIZABETH LEGG**, MSN, RN, CIC, infection control coordinator at The Mount Sinai Medical Center in New York City. "I hear from my colleagues that they tried and tried to get some information [about disinfectants] from EPA, but [the agency was] just not that helpful. And the manufacturers are in it for the business, so it's very difficult to depend on what they say about their products. I think a lot of us just don't know where to turn."

CDC recommended specific generic antimicrobials in its various infection control guidelines until 1983, but discontinued that practice to avoid "writing six or seven paragraphs about every product on the market," according to **MARTIN S. FAVERO**, PhD, chief of nosocomial infections, laboratory branch, in the CDC's Hospital Infections Program.

"In the past, [hospitals] more or less looked to CDC to make the choice for them, and specific generic recommendations are no longer in the guidelines," Favero told HIC. "I think that is appropriate, because there are so many different antiseptic and disinfectant formulations. It's no longer possible for us to recommend something like glutaraldehyde, because there are 12 different glutaraldehyde products out there . . . with different claims.

"The bottom line is that no one really believes there is much difference between those preparations, and the choice is actually left to the user," he added.

CDC's recommendations on antimicrobial agents may have been outdated even when they were first published in 1977, according to **ROBERT PINCO**, JD, a senior partner in the law firm of Finley, Cumble, Wagner, et al, in Washington, D.C. Pinco also is a pharmacist and former director of the FDA's OTC Drug Review.

"CDC was taking old information and going with it as if it was brand-new information, which it was not," said Pinco.

The last time CDC published antimicrobial recommendations in its guidelines was 1981. Those recommendations included the following.

- In a table called "Characteristics of antiseptic (antimicrobial) agents," the group recommended alcohols, 3%

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aqueous hexachlorophene, iodine compounds, iodophors, and 4% aqueous chlorhexidine. The table rated each agent's activity against bacteria.

- In a table called "Recommended agents for preparing the hands and cleaning the skin before nonsurgical and surgical procedures," CDC recommended handwashing agents (either soap and water or an antiseptic) and preoperative skin preparations (tincture of iodine or "antiseptics" were suggested).
- In a table called "Methods of sterilization and disinfection," CDC recommended high- or low-level disinfection (with appropriate agents), or sterilization methods for specific objects, such as lensed instruments.

Are those tables still applicable?

"Yes, but the problem is that there are things not listed on the tables that also work," Favero told HIC.

FRANK B. ENGLEY Jr, PhD, a member of the FDA's OTC Topical Antimicrobial Review Panel, disagrees. Engley is a microbiology professor at the University of Missouri in Columbia.

"They were just reprinting tables from the 1950s over and over," according to Engley.

Information 'easily misinterpreted'

The tables also were too easily misinterpreted, Engley added. For instance, alcohol is listed in the antiseptic tables as having "good" activity against gram-positive and gram-negative bacteria as well as Mycobacterium tuberculosis. Its "speed at killing sensitive bacteria" is rated as "fast." Some ICPs mistakenly took that information to mean alcohol was an effective skin prepping agent when used in a quick wipe, Engley told HIC.

"The truth is, alcohol is an excellent antimicrobial if used properly," he noted. "But if you take a little pledget of alcohol and wipe the deltoid area of your arm, and then give an injection there, the alcohol doesn't do a bit of good. It takes a minute and a half to two minutes for the alcohol to work," Engley continued.

"But then people began to use alcohol for prepping the skin for injection of IVs. And people forget that a number of factors are necessary for disinfectant action; you need the proper chemic the right concentration, and the right amount of contact time on the skin. Just quickly wiping the IV site with alcohol isn't sufficient."

Iodine only category I antiseptic

If the CDC's tables are not entirely accurate, then what does the FDA recommend in the way of antiseptics? In its first monograph on OTC antimicrobials in 1974, the OTC review panel placed one product in category I, the "proven to be safe and effective" antiseptic category: tincture of iodine. (Under "skin wound cleanser," there are four ingredients in category I; however, skin wound cleansers were not considered to be true antiseptics, according to the panel's findings in the first monograph. The only antimicrobials that should be considered truly antiseptic in action are patient preoperative skin preps, surgical hand scrubs, and skin antiseptics.) The second, most recent monograph (1978) does not place any additional ingredients in category I.

Why are the monographs so vague in their classification of antiseptics -- many of which have been recommended by some authorities since the 1930s? Engley says there are two reasons for the FDA categorization quandary:

- Lack of data from manufacturers on the safety and efficacy of their products.

"The panel looked at the data provided by the companies, and they said, 'Wait a minute. They didn't tell us enough; they didn't provide us with enough information. How can we make a scientific, educated decision based on what we've got?'

"The truth is, most companies thought we were kidding when we told them we were going to categorize their products, and they ignored us, or they sent us incomplete data," according to Engley.

Consequently, the majority of ingredients were placed in category III, indicating more data were needed to decide whether the product was safe and effective.

- The FDA is "scared to death" to make permanent decisions about the safety and efficacy of products, according to Engley.

"As soon as they come out with the final monograph, FDA is going to be taken to court with injunctions," he told HIC. "All of those companies that don't like what FDA has to say about [the classification of ingredients in] their products are going to send in injunctions. I know some companies are sitting on injunctions already, just waiting for the monograph to come out."

If the FDA won't or can't provide information about the safety and efficacy of skin antimicrobial agents, what about studying the "scientific literature," which CDC recommends in its most recent guidelines? **ELAINE LARSON**, RN, PhD, visiting chairwoman of clinical nursing and a researcher at Johns Hopkins University School of Nursing in Baltimore, has performed several clinical trials of handwashing products. She says that by reviewing "all the scientific literature we could find, from the National Library of Medicine to the American Chemistry Library," she has found "insufficient data" on the safety and efficacy of most of the active ingredients in handwashing agents. The most common problem with published studies is that they are too small.

"If you're looking at things like systemic toxicity, you don't have any power with a small sample size," Larson told HIC.

Study protocols are inconsistent

The evidence that companies submit to the FDA in hopes of making it to category I in the final monograph also is fraught with inconsistencies, according to Larson.

"Hardly any of the companies use the same protocols for studies," she said. "Investigators use so many different techniques for evaluating, even when counting the bacteria on the hands. There are no standardized techniques. The techniques that FDA recommends aren't often used by investigators."

Without much information to go by, ICPs are faced with the challenge of choosing antimicrobial agents for their facilities. Many are new formulations.

"I could do nothing but see salesmen for 40 hours a week if I wanted to," said **SANDRA PFAFF**, RN, BSN, CIC, infection control nurse at Strong Memorial Hospital in Rochester, NY. "But I don't care if their product kills every germ known to man. If personnel won't use a product because it's drying or irritating to their hands, then it's absolutely no good. And if companies can't back up [efficacy claims] with clinical trials and extensive studies, then I won't even consider their products."

(Companies that have formulated products with newer ingredients not listed in the monographs have filed "New Drug Applications" [NDAs] with the FDA's Office of Biologics, Anti-Infective Division. To receive a listing of new ingredients approved for safety and efficacy under an NDA, contact: FDA, Freedom of Information Staff, HFI-35, 5600 Fishers Lane, Room 12 A 16, Rockville, MD 20857.)

Disinfectant efficacy data incomplete

When it comes to hospital disinfectants, efficacy data may be just as difficult to come by as information on skin antimicrobials, according to **WILLIAM A. RUTALA**, PhD, a research associate professor in the Division of Infectious Diseases at the University of North Carolina School of Medicine, Chapel Hill. Rutala also is administrative director of hospital epidemiology at North Carolina Memorial Hospital in Chapel Hill.

There are "presumed deficiencies" in the AOAC (Association of Official Analytical Chemists) use-dilution test used by manufacturers to prove efficacy of their products for registration by the EPA, Rutala says. (See Infect Control 1984; 5:214-218.) Those deficiencies are most apparent when independent laboratories get different test results than manufacturers' laboratories, as is the case in Florida. About a third of the disinfectants tested by that state's laboratory have flunked the AOAC test, according to **STEVEN RUTZ**, administrator of the Pesticide Enforcement Section of the Florida Department of Agriculture and Consumer Services in Tallahassee. Florida is one of several states under contract with the EPA to evaluate disinfectants used in hospitals and other institutions. (See "Do disinfectants need tests for effectiveness?" HIC, March 1983, pp. 29-31.)

The more than 200 disinfectant samples a year that the state microbiology laboratory tests are already registered by the EPA. About 30% of those disinfectants (not all were from hospitals) flunked the AOAC test in 1984, the latest year for which figures are available, according to Rutz. Some of the same disinfectants that had initially passed the test when it was given by manufacturers to become registered by the EPA later failed the test in Florida's microbiology laboratory.

Rutz attributes those deficiencies to the many "variables" in the AOAC test, which can produce different results by different laboratories. (Rutz's division will answer questions about the efficacy of a particular disinfectant that has been tested. Contact: Florida Department of Agriculture and Consumer Services, Food Laboratory, 3125 Conner Blvd., Tallahassee, FL 32301.)

Is 'true data' from companies missing?

Many ICPs doubt that manufacturers submit "true data" to become registered by the EPA, or categorized by the FDA, according to Favero. He does agree that the AOAC test used on disinfectants is "totally inaccurate" because of at least 14 "uncontrolled" variables in the test. However, he does believe that "the industry is regulated," by the FDA and EPA, and that antimicrobials do perform as labeled. Like Rutala, Favero emphasized that most incidences of contamination are extrinsic -- from product misuse, or from not reading the label correctly.

"I know it's always a worry that certain companies might not be honest enough to supply FDA or EPA with true data," he told HIC. "Every meeting I go to, infection control people say, 'How can you trust companies -- they're such charlatans.' But the evidence doesn't really show that."

He cited recent doubt by ICPs about the mycobacteriocidal efficiency of a glutaraldehyde formulation, questioning whether it was "truly overformulated." The manufacturer claimed the formulation was effective for 14 days or longer. There also was concern that the formulation could not inactivate mycobacteria in 10 minutes, as claimed.

"It turns out that the company's claims were accurate, in spite of the fact that the original data came solely from the manufacturer," according to Favero.

(For a reprint of an article Favero published on antimicrobial agents in Manual of Clinical Microbiology, send a request for "Sterilization, Disinfection, and Antisepsis in the Hospital" to: Martin S. Favero, PhD, Hospital Infections Program, Centers for Disease Control, Atlanta, GA 30333.)

Short of doing their own research, which is not possible, how can ICPs really know if the products their facilities use are safe?

No easy answers, according to researcher

"I wish I had a brilliant answer to that question, but I don't," Rutala told HIC. "I think it's important for each ICP to evaluate data from individual sources. Try to find as many independent studies as possible. There are chapters in books that are helpful, but make sure the authors provide scientific support for their recommendations."

(Editor's note: HIC will report on the safety and efficacy of specific antimicrobials in next month's issue.)■

FDA sends monographs from 1970s when antiseptic data requested

What does the Food and Drug Administration send when it receives requests for information on the safety and efficacy of skin antimicrobials?

HIC made that request to the OTC Drug Evaluation Division of the Center for Drugs and Biologics, Office of Drug Standards. That division sent copies of two Federal Registers, dated September 13, 1974, and January 6, 1978, which contained the categorization of 19 "active ingredients." Those ingredients ranged from benzalkonium chloride to triple dye.

The registers consist of 80 pages of fine print, called "monographs," which summarize the extensive findings of two scientific panels. Those panels were made up of microbiologists, pharmacists, dermatologists, and other scientific experts, who reviewed laboratory and clinical studies on products and placed them in categories from 1972 to 1977.

Ingredients categorized in first monograph

In the 1974 monograph, the panel categorized ingredients as follows:

Category I. Conditions under which antimicrobial products are generally recognized as safe and effective and are not misbranded.

Category II. Conditions under which antimicrobial products are not generally recognized as safe and effective or are misbranded.

Category III. Conditions for which the available data are insufficient to permit final classification at this

The panel broke down the ingredients into the following classifications (only the first three agents listed below are considered to be true antiseptics by the panel, however):

- skin antiseptics;
- patient preoperative skin preparations;
- surgical hand scrubs;
- health care personnel handwashes;
- skin wound cleansers;
- skin wound protectants;
- antimicrobial soaps.

Most ingredients placed in category III

The majority of the active ingredients categorized by the panel were placed in category III (73 of 133). Forty-six of the ingredients were placed in category II; and only five were placed in category I (see related story, pp. 29-33). Sixteen of the products were not categorized "due to physical and/or chemical incompatibility in formulation."

The 1978 monograph contains responses to more than 100 questions and comments about the categorization of products in the first monograph. Most comments posed to the FDA in the second monograph were made by drug manufacturers. Common complaints concerned the costly testing process that FDA requires for product reclassification.

The second monograph also places additional ingredients not listed in the previous monograph into categories II and III, with extensive comments about the safety or efficacy of those ingredients. Also addressed in the second monograph are "final testing guidelines for safety and effectiveness" of OTC antimicrobials.

Because the FDA does not test OTC antimicrobials itself, manufacturers must submit safety and efficacy study data to the agency to be considered for reclassification in the "final monograph." That monograph will be compiled and released at an undisclosed date, according to an FDA official in the OTC Drug Evaluation Division.

But what about the majority of antimicrobials studied by the FDA panels, which were placed in categories II and III? According to **WALLACE GUESS**, PhD, a toxicologist and dean of pharmacy at the University of Mississippi in Oxford and former chairman of the FDA's antimicrobial panel, much of the information in the registers is outdated. For instance, the second monograph contains quite a bit of information about the toxicity of iodophor products, ranging from "burns on occluded skin" to changes noted in the thyroid function of patients when certain types of iodophors were used on open wounds.

Newer iodine products no longer toxic

However, "the irritation of iodine has been overcome by the use of the carrier molecule" in newer formulations. In addition, the possibility of systemic absorption has been corrected by using iodine molecules in complexed rather than free form, according to Guess.

When iodophors were first presented to Guess's panel, he told HIC, very little information was available on those products. "But as we raised more and more questions, . . . it became known that the iodophors are indeed complexed and are released over a period of time. They do act as skin antimicrobial agents, and without toxicity."

Guess also recently recommended to the FDA that para-chloro-meta-xylenol (PCMX) be placed in category I, instead of category III, where it was placed in the monographs due to a lack of data.

"In the early days, we had no data on the safety of PCMX," said Guess. "Then, as more and more data have come in and with the panels no longer in existence, I have reviewed all of the data [on PCMX], and I'm now convinced that it's a safe product."

Toxicity main concern of panel

Initial doubt about the safety rather than efficacy of products may be one reason many ingredients were not placed in category I, according to **MARY K. BRUCH**, vice-president for quality assurance, regulatory affairs, and life sciences at Dexide Inc., which manufactures PCMX products. Bruch also is former executive secretary in the FDA Division of Anti-Infective Drug Products and a member of the working group for the CDC's 1981 *Guideline for Hospital Environmental Control*.

When hexachlorophene was discovered to be highly toxic during the early 1970s, especially to newborns, the panel "realized that there was a product out there that people had not recognized could be toxic in such low levels. . . . No company -- and not many scientists -- had studied what happens if [hexachlorphene] is absorbed, distributed, and metabolized. So the panel had to say they didn't have enough information" to place many ingredients in category I, because of the fear of possible toxicity problems with other antimicrobials, Bruch noted.

FDA says no data available since 1978 monograph

Since the 1978 monograph, manufacturers have been providing FDA with updated safety and efficacy data continually in hopes of making it to category I, according to **FRANK B. ENGLEY Jr**, PhD, microbiology professor at the University of Missouri in Columbia and former OTC antimicrobial review panel member. But none of that information will be available to the public until the final monograph comes out, according to a spokesman in the FDA's Office of Drug Standards in the OTC Drug Evaluation Division.

"Until that final review is complete, and until all the material has been submitted for that review, then that information is just not available to the public," the spokesman said.

What about obtaining safety and efficacy data from the FDA's Freedom of Information (FOI) Office?

"When you write to Freedom of Information, they will give the letter to us to reply to, and you'll get the same information you would if you just wrote to us," according to the spokesman. The spokesman added that the FDA has recently devised a letter to explain the situation to people who request data that will be in the final monograph. The letter and the two existing monographs (copies of the *Federal Registers*) are the only information the OTC office will send.

Former director says new data is 'public record'

However, **ROBERT PINCO**, JD, senior partner in the Washington, D.C., law firm of Finley, Cumble, Wagner, *et al*, and director of the OTC Drug Review from 1974 to 1977, says updated safety and efficacy material is available to the public from the FDA.

Companies have submitted "plenty of material" in their attempts to move products from category III to category I, Pinco told *HIC*. "Clearly, there has been data submitted, which is a matter of public record."

Some companies have submitted thousands of pages of data, which FDA may not have had sufficient time or personnel to summarize yet. But the agency may also be dragging its feet for other reasons, according to Pinco.

"You realize as you get deeper into this, that's why the FDA has not been able to make up its mind," he added. "They've been very nervous. The data is not as good as they would like. And these are major, long-term, permanent decisions."

To determine exactly what FDA has available, *HIC* recently made a request to the agency's FOI office for information on safety and efficacy studies submitted by manufacturers since the 1978 monograph. We will report on what we receive from that office in an upcoming issue.

Write to FOI at the following address: Food and Drug Administration Freedom of Information Staff, HFI-35, 5600 Fishers Lane, Room 12 A 16, Rockville, MD 20857. ■

Regulation of disinfectants criticized by authorities

The Environmental Protection Agency can tell infection control practitioners whether a particular hospital disinfectant is registered or not. But it is up to the manufacturer to prove that its disinfectant is effective against a broad spectrum of organisms. The manufacturer must submit test data to the EPA for registration approval; the agency no longer tests the safety or efficacy of disinfectants on its own. (See related story, pp. 29-33.)

According to **ART CASTILLO**, a chemist and product manager in the agency's disinfectants branch, the words "EPA registered" on the label of a product called a "hospital disinfectant" mean that the product is effective against Salmonella choleraesuis, Staphylococcus aureus, and Pseudomonas aeruginosa.

EPA merely reviews data from companies

"To get a product registered, [companies] have to submit labels and efficacy data," Castillo added. "Our scientific people will review that material, and if they find that the microbiological efficacy data support the claims made for the product, we go ahead and register it. We approve the label."

But how is that label approved? By a scientist behind a desk, who reads safety and efficacy testing data provided by manufacturers. Although EPA used to test products in its laboratories -- both before and after registration -- the agency now merely evaluates a manufacturer's test claims before registering the product, according to Castillo.

Disinfectants with labels that claim to be effective against organisms other than the ones listed above, such as Mycobacterium tuberculosis or specific viruses, also must be supported by additional efficacy data against those specific organisms to become registered, Castillo added.

The authorities classify disinfectants differently, however. In a chapter of a book about antimicrobial agents[1], **MARTIN S. FAVERO**, PhD, of the CDC Hospital Infections Program, examines the efficacy of "commonly used disinfectants." Phenolic compounds are "corrosive," according to Favero, while iodophors are "somewhat unstable." On a scale of 0 to 4, aqueous glutaraldehyde is rated "3," while mercurial compounds are given a "0" for efficacy.

WILLIAM A. RUTALA, PhD, a research associate professor in the Division of Infectious Diseases at the University of North Carolina School of Medicine, Chapel Hill, says the incidences of contaminated disinfectants (and antiseptics) are on the rise, according to published reports. (See *Infection Control* 1984; 5:214-218.) For instance, between 1975 and 1979, there were 10 documented incidences of contaminated germicides in scientific literature. Nine such incidences were documented between 1980 and 1984. Of the four contaminated disinfectants reviewed by Rutala, all contained a species of Pseudomonas. (See "Disinfectants fail to meet manufacturers' claims, study finds," *HIC*, May 1982, pp. 66-67.)

Of 10 phenolic and quaternary ammonium compounds tested by Rutala using the AOAC use-dilution method (the same test companies use for efficacy data submitted to the EPA), the disinfectant consistently killed Staphylococcus aureus and Salmonella chloeraesuis. However, those disinfectants were "generally ineffective against P. aeruginosa," according to Rutala's research.

Rutala advocates "stricter control measures" by the EPA and FDA to prevent contamination of hospital germicides -- otherwise "we can confidently predict that additional reports will emerge" of contaminated germicides and subsequent nosocomial infections.

SEYMOUR S. BLOCK, PhD, bioengineering professor in the University of Florida's Chemical Engineering Department in Gainesville, is editor of *Disinfection, Sterilization and Preservation*[1]. Block said disinfectants are more likely to be extrinsically rather intrinsically contaminated -- and that hospital personnel should be careful and read labels precisely when preparing or diluting those products. In addition, items that are to be disinfected must be properly cleaned of surface debris first.

"Clearly, when you look at outbreaks in hospitals, it's a rare instance when an outbreak can be traced to a contaminated disinfectant," Block told *HIC*. "It's the conditions under which the products are used that are important."

However, disinfectants can be intrinsically contaminated, according to **FRANK B. ENGLEY Jr**, PhD, of the University of Missouri in Columbia. The two most common types of intrinsic contamination are improper manufacturing processes, such as pouring agents into contaminated containers, and actual failure of a product to perform as claimed. Subsequently, manufacturers have had to recall batches of their products, according to Engley. But the EPA is not "strict enough" with its regulation of manufacturers whose products have been found to be contaminated.

"A manufacturer can keep his product on the market for four or five years [after the product has been found to be contaminated]," Engley told *HIC*. "He can tell the EPA, 'Well, that batch was contaminated. I'll send you another sample,' and that could go on for years."

Consequently, Engley recommends that ICPs closely scrutinize the products their hospitals use by looking beyond EPA registration. Ask manufacturers for the data they used to substantiate label claims with EPA. Generally, the products most likely to live up to their claims are ones backed up by in-vivo tests, clinical trials using large numbers of people, and studies performed by at least two different hospitals or private laboratories.

For questions concerning the efficacy of a particular disinfectant, contact EPA, Juanita Wills, Branch Chief, Disinfectants Branch, Registration Division, (TS-767), 401 M St., Washington, D.C. 20460. Castillo said to specify the type of formulation, the name of its manufacturer, and the EPA registration number, if possible.

Reference

1. Favero MS. Chemical disinfection of medical and surgical materials. In: Block SS, ed. *Disinfection, Sterilization and Preservation*. Philadelphia: Lea & Febiger, 1983. ■

Reader Questions

Chief Consultant: **Peter Heseltine**, MD
Epidemiologist, Los Angeles County USC Medical Center, Los Angeles
Consultant Emeritus: **Calvin M. Kunin**, MD
Pomerene Professor and Chairman, Department of Medicine, Ohio State University School of Medicine, Columbus
Consultant: **John A. Washington II**, MD
Chairman, Department of Microbiology, Cleveland Clinic Foundation, Cleveland, OH
Consultant: **Linda Spencer**, RN, MPH
Coordinator, Hospital Infection Control Training, Emory University School of Nursing, Atlanta

Identifying employees at risk for TB a 'difficult challenge'

Question: How should infection control practitioners define exposure to tuberculosis? After caring for a patient with a cough in our emergency room, some employees were upset when it was discovered several days later that he had pulmonary TB. Should those employees be tested?

--Submitted by: An Illinois ICP.

Answer. Exposure to tuberculosis occurs whenever susceptible individuals are placed in a situation where they could inhale tubercle bacilli expelled into the air by an infectious source case. Despite that deceptively simple definition of exposure, identifying patients and employees who are at risk can be one of the most difficult challenges faced by infection control practitioners.

The key to successful identification of those exposed is knowing the nature of TB transmission and the ways in which characteristics of the source case, the environment, and the susceptible host interact, creating situations that may or may not be conducive to the transmission of infection. For example, it is important to establish whether the source case was potentially infectious, as well as when and where transmission to others may have taken place. Ask yourself these questions:

- Did the patient have pulmonary disease?
- Were sputum smear results positive?
- Was he or she coughing spontaneously?
- Was he or she taking effective medication?

What about the environment? Shared air space is essential for TB transmission, but close physical contact is not necessary.

Characteristics of the potentially exposed individuals also affect decisions about contact investigations, the most important characteristic being susceptibility, as indicated above. (For more information about TB transmission and factors to consider, see reference materials listed at the end of this response.)

Also consider whether or not exposed employees should have a skin test for TB. After consideration of the factors I've mentioned above, if any employee with a nonsignificant skin test is determined to be at risk of new TB infection, he or she should have one or more skin tests as part of a contact investigation. The timing of the tests is determined by how long ago the exposure occurred and whether each employee's skin test status at the precise time of the exposure was known.

For employees who are already known skin test reactors, the contact investigation would consist of an evaluation of the presence of TB symptoms. Any exposed individuals should also be evaluated for preventive therapy according to guidelines established by the American Thoracic Society and the Centers for Disease Control (see references below).

When a case of TB occurs, it is worth the effort to correctly identify employees and patients who were (and who were not) truly exposed. Doing so can put a reasonable limit on the work load created by a contact investigation and can mean the different between the success or failure of efforts to control the spread of a tuberculosis outbreak.

--Guest consultant: **MARY DEVEREAUX HUTTON**, RN, MPH, Centers for Disease Control, Tuberculosis Control Division, Atlanta.

Selected references

1. American Thoracic Society, American Lung Association. Treatment of tuberculosis and other mycobacterial diseases, and Control of Tuberculosis. Am Rev Resp Dis 1983; 127:790-796; 128.336-342.

2. Centers for Disease Control. Guideline for Isolation Precautions in Hospitals and Guideline for Infection Control in Hospital Personnel, 1983. U.S. Department of Health and Human Services publication (CDC) 83-8314.

3. Division of Tuberculosis Control, CDC. Guidelines for Prevention of TB Transmission in Hospitals, 1982. HHS publication (CDC) 82-8371.

4. Snider D, Cauthen G. Tuberculin skin testing of hospital employees: Infection, "boosting," and two-step testing. Am J Infect Control 1984; 12:305-311.

48-hour IV piggyback sets safe if proper precautions are taken

Question: Many of our patients receive intravenous antibiotics through a capped needle or cannula ("INT"), delivered via a single administration set. Those sets are discarded after each use, which makes their cost quite high.

Instead of returning to a piggyback/continuous infusion system, could administration sets be safely disconnected from the INT, covered with a new, sterile, capped needle, left hanging on the IV pole in the patient's room, and reused after 48 hours? Or will this alternative measure significantly increase in-line bacterial contamination in those patients?

--Submitted by: **PATTI EMMETT**, RN, BS, CIC, infection control nurse, Community Hospital of the Monterey Peninsula, Monterey, CA.

Answer: The safety of 48-hour interval changes for IV administration sets has been proved[1-3]. Also, the current Centers for Disease Control Guideline for the Prevention of Intravascular Infections includes piggyback tubing in its recommendations for 48-hour tubing changes. Piggyback tubing may be used intermittently, according to the guideline; so may the intermittent infusion setup you have described.

Your proposed method is practical and does not appear to violate any infection control principles. However, I would stress the importance of the following two factors:

- Immediately after use, the tubing should be covered with a new, sterile, capped needle.
- The IV fluid must be changed every 24 hours without fail. The best way to ensure those changes take place is to have the nursing staff write the dates the infusions were begun on both the administration set and the IV bottle.

--Guest consultant: **LORETTA FRAWLEY**, RN, MSN, CIC, infection control nurse, Veterans Administration Medical Center, Decatur, GA.

Selected references

1. Buxton AE, Highsmith AK, Garner JS, et al. Contamination of intravenous infusion fluid: Effects of changing administration sets. Ann Intern Med 1979; 90:764-768.

2. Bond JD, Maki DG. Safety of changing delivery systems at longer than 24-hour intervals. Ann Intern Med 1979; 91:173-178.

3. Gorvea HF, Snydam DR, Delaney A, et al. Intravenous tubing with burettes can be safely changed at 48-hour intervals. JAMA 1984; 251:2112-2115.

Scrub suits not 'cleaner' than wearing uniforms in ER

Question: Our emergency department personnel have requested that they be allowed to wear scrub suits instead of their own uniforms while on duty. Do you have any recommendations for or against wearing scrubs in the ER? Does wearing scrubs instead of uniforms have anything to do with infection control?

--Submitted by: **BECKY GOECKE**, RN, infection control coordinator, St. Rita's Medical Center, Lima, OH.

Answer: I know of no studies comparing nosocomial infection rates related to the type of clothing worn in patient care settings, such as intensive care units or emergency rooms. Opinions on the matter are, therefore, just that -- opinions.

I think the answer depends on the reasons your ER personnel want to wear scrubs. Those reasons probably are as follows:

- It is less expensive than buying uniforms.
- Personnel consider scrubs "cleaner" than their own uniforms.
- Scrubwear is "prestige" apparel in some people's minds.

Some institutions find the extra expense involved in buying scrub dresses and suits for staffs objectionable. If the expense is not objectionable to the institution, then I think the staff should be able to save themselves the cost of buying and laundering their own work clothing. Some institutions have solved part of the expense problem by providing scrubs at cost to their personnel, then assuming the cost of laundering the apparel.

However, for staff who wish to wear scrubwear because it is "cleaner" than uniforms (which I doubt), I believe there should be two stipulations involved in the wearing of the scrubs:

- Everyone in the area under question should be required to abide by the dress code decided upon by the unit's personnel.
- Scrubwear must be laundered by the hospital laundry and should not be worn outside the hospital grounds.

The reasons for the above recommendations are twofold. First, if the staff feels that scrubs are "cleaner" than nurses' uniforms, then it follows that the hospital laundry can provide a better wash than laundry done at home. And second, when scrubwear is taken off the premises, it tends to "disappear," making it very expensive for a hospital to maintain the necessary supply.

So, although the use or nonuse of scrubwear does not really affect infection control, other issues do exist. I suggest that you discuss those issues carefully before making a decision at your institution.

--Guest consultant: **INGE GUREVICH**, RN, MA, infection control practitioner, Winthrop-University Hospital, Mineola, NY. ■

Sources of Information

• *Reviews of Clinical Infectious Diseases, 1985*. $39.50; order code 791231. Grune & Stratton Inc., Orlando, FL 32887.

This review summarizes almost 700 articles from recent issues of journals such as *The Lancet* and *The Journal of Infectious Diseases*. Emphasis is placed on clinical applications for infection control practitioners, clinical and microbiology laboratory workers, epidemiologists, and clinical bacteriologists. The text includes chapters on antimicrobial agents, infection prevention, bacterial diseases, mycoses, and viruses.

• *Good Hospital Practice: Steam Sterilization Using the Unwrapped Method (Flash Sterilization)*; order number AAMI SSUM-10/85. $28 for members of the Association for the Advancement of Medical Instrumentation; $43 for nonmembers. Dawn Boots, AAMI, 1901 North Fort Myer Drive, Suite 602, Arlington, VA 22209.

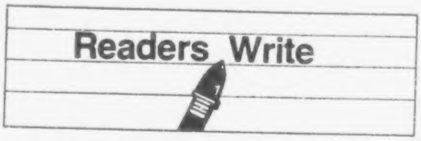
These guidelines were recently approved by the standards board of AAMI. They include information on ensuring sterility of items steam-sterilized by the unwrapped method in either gravity displacement sterilizers or prevacuum sterilizers. Tips on handling items safely, controlling infection, and maintaining sterility of processed items also are included.

• *Managing Hospital Infection Control for Cost Effectiveness*. $32.50 for nonmembers; $26 for AHA members. American Hospital Association, P.O. Box 96003, Chicago, IL 60693.

This manual, by Robert Haley, MD, includes illustrations, charts, work sheets, and checklists to cut costs in infection control programs.

• *Reports on AIDS*. $10.50 for paperback book; $8.95 for microfiche. National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161.

This publication is a compilation of articles on acquired immunodeficiency syndrome from CDC's *Morbidity and Mortality Weekly Report* from 1981 to 1985.■



Readers Write

Sterile containers used for 'leakproof' qualities

Dear Editor: I was pleased to read the answer given by one of your consultants, John A. Washington II, MD, in a Reader Question in the November 1985 issue of *HIC* (pp. 139-140). The question, titled "Containers for stool specimens should be leakproof, not sterile," asked whether sterile containers are necessary for transporting stool specimens to the laboratory.

Dr. Washington replied that clean containers are sufficient because sterility of the container is not necessary for stool specimens.

However, at our institution, like in many others, the nonsterile containers used are not leakproof, and they do not have a screw cap. Consequently, we must use sterile containers (which do have a screw cap) to assure safety when transporting stool specimens to the laboratory, even though sterility of the specimen is not necessary.

--Submitted by: **ELISE OYDNA**, MT, SH, SM (ASCP), supervisory microbiologist, Veterans Administration Medical Center, Brooklyn, NY.

Hospital traces infections to transparent IV dressings

Dear Editor: I am writing in regard to the recent article published in *HIC* concerning the use of transparent dressings on IV sites. (See "Studies are cited on efficacy of transparent adhesive dressings," *HIC*, January 1986, pp. 3-6.)

At our hospital, we have seen an increase in infections that we believe is related to the use of transparent adhesive dressings (TADs). We began using TADs in June 1983. From January to May of that year, no IV-associated infections were reported. However, from June to September, four patients acquired IV-site infections.

In 1984, we discovered 17 patients had IV site infections; seven acquired secondary bacteremias. Of those 17 affected patients, nine were infected with Staphylococcus epidermidis.

In January 1985, we audited the infected patients' charts. When we read in the April issue of HIC about Dr. Patrick Joseph's findings [from research on TADs at Merritt Peralta Medical Center in Oakland, CA], we immediately discontinued the use of TADs on IV sites. (See "Transparency of the polyurethane dressing not significant advantage," April 1985, pp. 50-51.)

We made that decision in May of last year; since that time, we have had no IV-related infections.

--Submitted by: **GAYLE ROSENBERG**, RN, CIC, infection control coordinator, St. Agnes Hospital, Fond Du Lac, WI. ■

Risk of rotavirus infection increases with length of stay

The chance that infants and toddlers will acquire rotavirus nosocomially increases the longer the patient is hospitalized, according to research done at the University of Maryland in Baltimore.

From January through March of 1985, more than 150 patients 24 months old or younger who were admitted to the infant ward at the university's hospital were tested every other day for excretion of rotavirus (RV). RV was found in the stools of 34 patients upon admission. Eight of those RV-positive patients were asymptomatic during their entire hospitalization, according to the researchers, who presented their findings at the Interscience Conference on Antimicrobial Agents and Chemotherapy.

Of 118 patients who were rotavirus (RV) negative on admission, 24 (20%) acquired RV. Infants most likely to acquire nosocomial RV were those who had room contact with another patient known to excrete RV. Asymptomatic RV occurred most often in patients younger than one month of age.

Research results also showed a 2% per day risk of acquiring RV during hospitalization. The lowest risk for acquisition occurred in patients who were hospitalized for no longer than two days.

"The occurrence of asymptomatic excreters and the high frequency with which such excreters are associated with transmission of RV raise questions about the adequacy of current infection control guidelines" concerning rotavirus, the researchers concluded.■

MMWR Update

Increase in measles cases due to lack of immunization

Since 1982, the number of cases of measles in the U.S. has increased slightly each year, according to a recent issue of Morbidity and Mortality Weekly Report (1986; 35:1-4). About 900 more cases of measles occurred in 1985 than in 1984 -- a 2.4% increase.

Nosocomial measles transmission still comprises a small percentage of U.S. cases each year, according to the report. Only about 70% of the overall measles cases reported to the Centers for Disease Control last year specified the setting of transmission for the disease. Out of those, the most frequent setting of transmission was school (71.9%), followed by the home (10%). Medical settings comprised 3.3% of cases, as did day-care centers. About 10% of cases occurred in church, summer camps, and other community settings.

The numbers of measles cases since 1981 have been as follows:

- 1981 - 3,124;
- 1982 - 1,714;
- 1983 - 1,497;
- 1984 - 2,534;
- 1985 - 2,704.

To decrease the number of preventable measles cases, "greater efforts need to be directed" to the preschool age group, which often is not reached by mandatory immunization school laws.

"Continued enforcement of current school immunization laws is important for further reduction of measles in the United States," the report concluded.

Updated AIDS statistics show related diseases are changing

As of January of this year, about 16,500 patients have been diagnosed with acquired immunodeficiency syndrome in the U.S., a recent issue of Morbidity and Mortality Weekly Report states (1986; 35:17-21). More than half of those adult patients (51%) have died since AIDS reporting began in 1981; 59% of the 231 children with AIDS have died.

However, "significant changes have occurred in the distribution of specific diseases reported," the report states. The most common opportunistic infection among patients is Pneumocystis carinii pneumonia (PCP), and the incidence of PCP is rising compared to other opportunistic diseases, such as Kaposi's sarcoma. Before January 1984, PCP accounted for 35% of the diagnosed AIDS-related diseases. But in 1985, PCP was reported in 47% of patients with AIDS.

The incidence of Kaposi's sarcoma is decreasing. Before December 1984, Kaposi's sarcoma was reported in 21% of AIDS cases; by 1985, that figure had dropped to 13%.

Of the 16,458 AIDS cases reported to the Centers for Disease Control since 1981, the overall incidence of opportunistic disease as been as follows:

- 63% - PCP;
- 24% - Kaposi's sarcoma;
- 14% - candida esophagitis;
- 7% - cytomegalovirus infections;
- 7% - cryptococcosis;
- 4% - chronic herpes simplex;
- 4% - cryptosporidiosis;
- 3% - toxoplasmosis;
- 3% - other diseases.

Between 1982 and 1983, a 184% increase in AIDS cases was reported, but that percentage has since decreased consistently, the report states. Between 1984 and 1985, the number of AIDS cases increased 115%; in 1985, only an 84% increase occurred.

However, the report notes that some current patients with AIDS may have been exposed to HTLV-III/LAV as long ago as seven years, prompting CDC to warn that "longer incubation periods cannot be excluded." Because of the long incubation period, transfusion-associated AIDS cases will continue to occur, even though the current blood supply is tested for HTLV-III/LAV antibodies.

The report concludes that studies on the incidence and prevalence of HTLV-III/LAV infection are needed to determine whether current cases that meet the AIDS case definition "accurately reflect the distribution of infected persons."

"Persons meeting the AIDS case definition are only a small percentage of all persons infected with HTLV-III/LAV," according to the report. ■

Penicillin-resistant pneumococcus discovered in New York hospitals

Penicillin-resistant strains of Streptococcus pneumoniae are occurring in New York City hospitals, according to the city's health department.

At one city facility -- the Brooklyn Veterans Administration Hospital -- nine patients had positive pneumococcal cultures with "absolute resistance to penicillin" in a 1983 to 1984 study, the health department notes in its monthly bulletin, "City Health Information."

At the Brooklyn VA, isolates were obtained from throat cultures of six asymptomatic patients, who were believed to be colonized with S. pneumoniae. Three isolates also were obtained from sputum specimens of symptomatic patients.

Those nine isolates were found to be resistant to penicillin G, oxacillin, mezlocillin, cefazolin, ceftriaxone, tetracycline, chloramphenicol, and trimethoprim-sulfamethoxazole. Isolates were sensitive to erythromycin, clindamycin, and rifampin.

No "common source" was discovered for the nine isolates, which were "apparently related," the publication states.

As a result of those findings, the health department now recommends the following procedures for hospitals with patients who have resistant pneumococcal isolates:

- Test pneumococcal isolates for penicillin susceptibility from both sterile and nonsterile body sites.
- Do not administer additional antibiotics to infected patients.
- Use the disk diffusion method with a 1-mg oxacillin disk for testing penicillin susceptibility in pneumococci. (See N Engl J Med 1985; 313:615-617.) Medicine 1985; 313:615-617.)

Recommendations also include notifying the health department of absolute penicillin-resistant pneumococcus strains and sending the organism to the city laboratory for verification.■

Education Forum

By: **Marguerite M. Jackson**, RN, MS
Director, Epidemiology Unit
University of California Medical Center, San Diego

Multiple-choice test helps evaluate learner knowledge

One of the most popular forms of evaluating learner knowledge is the multiple-choice test. Most standardized tests use this form, as do national specialty tests for nurses, microbiologists, and other health professionals. The multiple-choice test can be helpful when presenting an inservice program on infection control.

When devising a multiple-choice test for an inservice presentation, consider using introductory questions or incomplete statements to introduce a set of answers. For example, an introductory question might read as follows: "Which of the following is a direct mode of transmission?" An incomplete statement, such as "The most important measure to reduce the risk of cross-contamination between patients is:" may also be used.

Finding enough appropriate response options for each question in multiple-choice tests can be difficult. Questions should be concise, or each reader may interpret them differently.

To make multiple-choice questions clear and simple, follow these tips:

- Avoid negative wording, which can be easily misinterpreted by the reader. For instance, use the word "likely" instead of the term "not unlikely."
- Provide a response that competent critics agree is the best answer. Ask your colleagues to review test items to eliminate ambiguity.
- Make sure each response agrees grammatically with the question. For instance, use the term "a(an)" when phrasing an incomplete question which has responses that begin with both vowels and consonants.
- Make the responses plausible and attractive to test takers. If each response seems reasonable, the test will be more difficult, and you will be able to discriminate between learners who really know the information and those who are guessing at the answers.
- Avoid using the phrases "none of the above," or "all of the above." Test takers know that those options are often the correct answer, and they will respond to that option whether they know the material or not.
- Make each response about the same length. Test takers will often choose the longest response as a clue to the right answer.
- Do not use the words "always," "only," and "never." Most test takers can find exceptions to statements using those words, thereby making the question difficult for you to defend.
- Do not place the correct answer in the same position frequently. For example, if you use four response options (a,b,c,d), rotate the correct answers between those four options. If you frequently use the same option for the correct answer, test takers will be able to guess the correct answer by the letter placement of other responses.

A well-designed multiple-choice test can help you determine how well you presented material and how well your audience understood it.■

Journal Review

By: **Charles P. Craig**, MD
Chairman, Department of Internal Medicine
Albert Einstein Medical Center
Philadelphia, PA

American Medical Association Panel Report: Pertussis vaccine injury. JAMA 1985; 254:3083-3084.

The administration of pertussis vaccine has been controversial because of recognized side effects associated with the vaccine. However, refusing to immunize is not the answer, according to this report. In Great Britain, wholesale abandonment of routine infant immunization had disastrous effects; pertussis repidly became epidemic among young children, and a number of them died. As proponents of preventive medicine, infection control practitioners should be aware of incidents such as those and weigh the consequences before deciding not to immunize.

●

Ho DD, Rota TR, Schooley RT. Isolation of HTLV-III from cerebrospinal fluid and neural tissues of patients with neurologic syndromes related to acquired immunodeficiency syndrome. N Engl J Med 1985; 313:1493-1497.

This article describes the isolation of the AIDS virus from spinal fluid and nerve tissue. It merely reiterates the importance of handling body fluids and specimens carefully because they could be potentially infected with HTLV-III/LAV. Proper precautions should be taken by personnel who handle spinal fluids, surgical or autopsy specimens, or nerve tissue.

●

Murray HW, Hillman JK, Rubin BY. Patients at risk for AIDS-related opportunistic infections. N Engl J Med 1985; 313:1504-1509.

Clinical presentations associated with HTLV-III/LAV infection are lumped together under the term "AIDS-Related Complex" (ARC). This article presents the challenge of determining which HTLV-III/LAV-positive patients are at risk for developing full-blown AIDS. The authors have identified which patients with ARC are most likely to develop AIDS -- such as patients with thrush and abnormal T-lymphocyte responses to standard indirect immunofluorescence assay testing. If confirmed, that test could be very useful in managing individuals with early manifestations of AIDS.

●

Francis DP, Petricciani JC. The prospects and pathways toward a vaccine for AIDS. N Engl J Med 1985; 313;1586-1590.

Will a vaccine for AIDS be developed? The answer is undoubtedly "yes," but the timing of a vaccine is not yet clear. However, the pathways investigators will take to develop an AIDS vaccine are reasonably well defined, as this concise article shows.

●

Lathan RH, Wong ES, Larson A. Laboratory diagnosis of urinary tract infection in ambulatory women. JAMA 1985; 254:3333-3336.

When physicians evaluate patients in the hospital to determine whether they have nosocomial infections, they frequently have to rely on admission urinalysis reports as baseline data. If the urinalysis was normal and the patient becomes infected, the UTI is considered nosocomial. But if the urinalysis showed an increased number of white blood cells, the evidence for nosocomial UTI is less convincing. This article substantiates a long-standing suspicion among ICPs that looking for pyuria is a reasonably specific and efficient way to screen for UTI -- thus validating the use of pyuria as baseline information.

●

Brady MT, May R. Premortem isolation of Saint Louis encephalitis virus: Case report and implications for hospital and laboratory personnel. Pediatr Infect Dis 1985; 4:548-549.

Isolating the virus of St. Louis encephalitis (SLE) from patients with the disease is often difficult. The authors of this article suggest that, because the saliva of patients with SLE contains the SLE virus, contact or secretion isolation precautions should be practiced when caring for those patients.

●

George WL, Nakata MM, Thompson J. Aeromonas-related diarrhea in adults. Arch Intern Med 1985; 145:2207-2211.

A significant number of adults have infectious diarrhea for which no cause can be found. The authors of this article report an abundance of patients with undiagnosed diarrhea, and they suggest that Aeromonas is the responsible organism. However, not much is known about how Aeromonas is acquired, indeed, it is present in the soil and water. Until more is known about the organism and how it is transmitted, it can merely be considered as a possible causative pathogen.

●

Seale L, Jones CJ, Kathpalia S. Prevention of herpes virus infections in renal allograft recipients by low-dose oral acyclovir. JAMA 1985; 254:3435-3438.

Herpes virus infections occur often in patients who have had kidney transplants. Although not life-threatening, herpes infections cause discomfort to the patient and may delay healing. Immunosuppressive drugs may cause infections to reactivate in those patients. If the infection causes a fever, it could make diagnosis of other opportunistic infections more difficult. This article points out that most herpes reactivations in kidney transplant recipients can be prevented with oral acyclovir, thus simplifying the early postoperative care of those patients.

Coming in future months:

■ More advice on choosing hospital antimicrobials ■ When are masks necessary in the OR? ■ Cleaning up blood spills with hypochlorite

ANALYSES OF DISINFECTANTS

FLORIDA DEPARTMENT OF AGRICULTURE & CONSUMER SERVICES

TYPE SAMPLES	FISCAL 80-81	FISCAL 81-82	FISCAL 82-83
State Enforcement	63	109	40
EPA Enforcement	102	204	34
State Purchasing	17	18	5
Company	-	3	7
TOTALS	182	334	86

FLORIDA DISINFECTANT ENFORCEMENT PROGRAM

FISCAL YEAR	NO. SAMPLES	% INEFFECTIVE
68-69	8	25%
69-70	201	32.8%
70-71	347	30%
71-72	265	21.9%
72-73	118	28.8%
73-74	201	21.9%
74-75	173	18.5%
75-76	157	9.6%
76-77	136	13.2%
77-78	153	16.3%
78-79	140	17.9%
79-80	106	18.9%
80-81	202	18.8%
81-82	289	24.2%
82-83	86	-
83-84	234	17.9%
84-85	264	23%
85-86	244	23%
TOTAL	3,324	

ANALYSES OF DISINFECTANTS

FLORIDA DEPARTMENT OF AGRICULTURE & CONSUMER SERVICES

FISCAL YEAR	NO. SAMPLES	% INEFFECTIVE
83-84	234	17.9%

TYPE SAMPLES	FISCAL 83-84
State Enforcement	138
EPA Enforcement	76
State Purchasing	17
Company	3
TOTALS	234

FISCAL 83-84

	Liquid		Spray	
	No.	%*	No.	%*
Quaternary ammonium	128	18%	27	14.8%
Phenolic	38	34.2%	11	0
Other	28	7.1%	2	0

*Ineffective percentages shown

ANALYSES OF DISINFECTANTS

FLORIDA DEPARTMENT OF AGRICULTURE & CONSUMER SERVICES

TYPE SAMPLES	FISCAL 84-85	FISCAL 85-86
State Enforcement	78	45
EPA Enforcement	179	185
State Purchasing	7	14

Number of samples	264	244
% Ineffective	23%	23%

Type of samples		% Ineffective		% Ineffective
Quaternary	206	15%	200	14%
Phenolic	58	19%	44	38%

Senator SARBANES. Thank you very much, Ms. Rhodes.
Mr. McQuade.

STATEMENT OF WALTER J. McQUADE, DIRECTOR OF REGULATORY AFFAIRS, SURGIKOS, INC.

Mr. McQUADE. Mr. Chairman, Congressman Scheuer, my name is Walter McQuade, I'm director of regulatory affairs at Surgikos, Inc. With me today is Theodore Wendt. Mr. Wendt is a Ph.D. microbiologist and is responsible for microbiological and analytical services. With your permission, Senator, I'd like to have Mr. Wendt to join me here.

Senator SARBANES. That's fine. Certainly.

Mr. McQuade. Mr. Wendt and I both welcome the opportunity to testify on Federal standards for hospital disinfectants. We believe there is a need for closer Federal scrutiny of hospital disinfectants for two reasons.

First, we believe the definition of "disinfectant" used by the EPA is inadequate.

Second, in light of scientific advances over the last 20 years, some of the current test methods relied upon by the Agency to show efficacy of disinfectants are inadequate, and the process presently required to improve or replace these test methods is both lengthy and cumbersome.

With regard to the definition of disinfectant, there is a dichotomy between EPA's definition and the user's understanding of that term. On the one hand, in order to label a product as a hospital disinfectant, EPA allows the registrants to conduct only the AOAC use-dilution test against three specified vegetative bacteria.

On the other hand, Webster's definition of disinfectant—"a chemical that destroys vegetative forms of harmful microorganisms but not ordinarily bacterial spores"—is also the basic definition used by health care professionals. Neither in the dictionary nor in medical texts is the definition limited to the common vegetative bacteria specified in the AOAC use-dilution test. But rather, the term used is "harmful microorganisms," which includes several groups of organisms for which efficacy testing is not required using EPA's definition.

It should be understood that activity against one category of bacteria does not support the assumption of effectiveness against other major groups of organisms.

Any product which claims effectiveness as a hospital disinfectant should be required to inactivate not only the three specified bacteria, but also pathogenic fungi, Mycobacterium tuberculosis, and hydrophilic and lipophilic viruses. Such a requirement would seem prudent, because these microorganisms constitute a significant health risk to debilitated patients, and it is impossible for the hospital user to identify contaminating organisms on equipment prior to disinfection.

With regard to the second point, Mr. Chairman, the EPA relies primarily on test methods developed and standardized by the Association of Official Analytical Chemists, the AOAC, in order to determine efficacy of hospital disinfectants. Our prepared statement presents in some detail the process by which outdated AOAC methods are modified and replaced.

Suffice it to say, this process may take several years to complete, which is too long to be responsive to the needs of the registrant, regulator or users.

To illustrate the problems in this process, we can examine the AOAC TB test and the process my company has gone through to modify or replace it. During the mid-1970's, Surgikos began to develop a second-generation disinfectant product. When we attempted to gauge our progress in formulation development using the AOAC test for tuberculocidal efficacy, we obtained inexplicable and contradictory results. Specifically, our contract laboratories had been asked to test several formulae of the new product. Each was the same except for the level of active ingredient, which varied from one-eighth of 1 percent to about 3 percent glutaraldehyde. We were amazed to receive results indicating that the formula with one-eighth of 1 percent glutaraldehyde passed the AOAC TB test, but the 3 percent solution failed.

As a result of these incomprehensible results, we decided to develop an inhouse testing capability. We then began our investigation of the AOAC TB test.

By 1983, we had identified the following faults in the AOAC test:

First, the existing AOAC tuberculocidal method precludes any control over the starting population which has been found to be highly variable. This greatly affects the time required to totally kill the test organisms.

In addition, there is a pronounced tendency for microorganisms to be washed off the carriers into the disinfectant, thus effectively reducing the potential recovery of viable bacteria.

Second, the mycobacteria used as the test organism is very sensitive to the temperature of disinfection, which is frequently poorly controlled, due to the use of biosafety hoods and other equipment during the performnance of this test.

Moreover, all of the faults found in the AOAC test tend to increase the likelihood of accepting a weak disinfectant but not of rejecting one which is, in fact, efficacious. In other words, the errors tend to be in the direction of greatest possible risk of failure to disinfect.

The development of a new quantitative TB test took place over a period of 3 years, using Surgikos laboratory personnel as well as contracted expertise at the Trudeau Institute at Saranac Lake, New York, and the National Jewish Hospital located in Denver, Colorado. The studies showed that the quantitative method is reproducible and that the test organisms are very representative of the pathogenic strains of M. tuberculosis causing illness in humans.

The new quantitative test method was presented to the EPA in March 1983. The EPA's comments and recommendations to us were reviewed and incorporated into this new test method and the modified document was returned to the Agency in August 1983.

The new method continues in the standard AOAC approval process. The interlaboratory collaborative study will begin shortly. We anticipate that this process, which began in 1978 with the appointment of the associate referee, will require at least 1 more year. In the meantime, the existing inadequate AOAC TB test is allowed to be used in support of registrations.

Many of the problems which we have encountered during the development of the new quantitative TB test method might have been avoided had the Agency's Beltsville laboratory been in operation. The laboratory could have served as a focal point for evaluation of proposed test modifications rather than the existing and somewhat cumbersome AOAC procedure. Had this option been available to us, we believe that questions about the TB test method would have been resolved about 3 years ago.

The reopening of the Beltsville laboratory, in conjunction with a revised definition of hospital disinfectant, could make a significant contribution in the areas of verification of registration testing, enforcement activity, and improving the accuracy of disinfectant labeling as understood by users.

In conclusion, we believe the regulatory process will be enhanced by the Agency's use of the commonly accepted definition of hospital disinfectant, and by speeding the process by which EPA verifies and approves modifications to acceptable testing procedures.

Mr. Chairman, we wish to commend the committee for identifying and shedding light on these problems. Thank you very much, sir.

[The prepared statement of Mr. McQuade follows:]

PREPARED STATEMENT OF WALTER J. McQUADE

My name is Walter McQuade. I am the Director of Regulatory Affairs at SURGIKOS, INC., which is a subsidiary of Johnson & Johnson. For the past twenty-five years, our company has manufactured disinfectants and sterilants for medical instruments and appliances.

With me is Theodore Wendt. Dr. Wendt holds a Ph.D. in microbiology. He is the Manager of Microbiology and Analytical Services at SURGIKOS. We welcome the opportunity to testify on federal standards and testing on hospital disinfectants.

We believe there is a need for closer federal scrutiny of hospital disinfectants for two reasons:

1. The definition of "disinfectant" used by EPA is inadequate.

2. In light of the scientific advances of the last twenty years, some of the current test methods presently relied upon by EPA to show efficacy of disinfectants may be inadequate, and the process presently required to improve or replace these test methods is lengthy and cumbersome.

Definition of Disinfectant

There is a dichotomy between EPA's definition of disinfectant and the user's understanding of that term. In order to label a product as a hospital disinfectant, EPA allows registrants to conduct only the AOAC Use-Dilution Test against three specified vegetative bacteria -- *Staphylococcus aureus*, *Salmonella choleraesuis*, and *Pseudomonas aeruginosa*. It is not necessary to test efficacy against pathogenic fungi, hydrophilic and lipophilic viruses, or *Mycobacterium tuberculosis*.

Webster's definition of disinfectant -- ". . . a chemical that destroys vegetative forms of harmful microorganisms but not ordinarily bacterial spores" -- is also the basic definition contained in medically oriented text books used by health care professionals and others involved in purchasing these products. Neither in the dictionary nor in medical texts is the definition limited to the common vegetative bacteria specified in the AOAC Use-Dilution Test, but rather, the term used is *harmful microorganisms*, which includes several groups of organisms for which efficacy testing is not required using EPA's definition.

It should be understood that activity against one category of bacteria does not support the assumption of effectiveness against other major groups of organisms. Thus, a product labeled as a "hospital disinfectant," without other claims, need not have been shown to be effective against a substantial number of groups of pathogenic organisms.

Any product which claims effectiveness as a hospital disinfectant should be required to inactivate not only the three specified bacteria, but also pathogenic fungi, Mycobacterium tuberculosis, and both hydrophilic and lipophilic viruses. Such a requirement would seem prudent because these microorganisms constitute a significant health risk to a debilitated patient, and it is impossible for the hospital user to identify contaminating organisms on equipment prior to disinfection.

Test Methods Relied Upon by EPA

I would like to relate our experience with the development of a new test for determining the tuberculocidal effectiveness of disinfectants to illustrate what we see as a problem with the present regulation of disinfectants. I'll begin with a brief description of the process by which improved test methods used to develop data to support efficacy claims are developed.

Under current procedures, EPA relies primarily on data from test methods developed and standardized by the Association of Official Analytical Chemists -- or AOAC -- to determine efficacy of hospital disinfectants. The modification or replacement of an existing AOAC test method which has been determined to be inadequate begins with the appointment of an Associate Referee for the method in question. The Associate Referee, who is a scientist from industry, academia or government, develops intralaboratory data in support of a modified or replacement method. Once the data is collected and analyzed to the satisfaction of the General Referee, who has traditionally been an EPA employee, the method is submitted to the AOAC to verify its suitability and readiness for collaborative study. The collaborative study determines the variation in results which will occur between laboratories conducting this test -- or the interlaboratory reproducibility of the method. Upon successful completion of the collaborative study, the modified or replacement method is then submitted to the AOAC for consideration and approval at its annual meeting. If approved, the method is published in the collected methods of the AOAC as an Official Final Action Method. That method then becomes accepted by EPA and others as capable of producing valid scientific data. This entire process may take several years to complete, which is too long to be responsive to the needs of the registrant, regulator, and users.

Development of a New Tuberculocidal (TB) Test

During the mid-1970's, SURGIKOS began to develop a second-generation disinfectant product. When we attempted to gauge our progress in formulation development using the AOAC test for tuberculocidal efficacy, we obtained inexplicable and contradictory results. Specifically, our contract laboratories had been asked to test several formulae of the new product. Each was the same except for the level of active ingredient, which varied from 1/8 of 1% to 3% glutaraldehyde. We were amazed to receive results indicating that the formula with 1/8 of 1% glutaraldehyde passed the AOAC TB test, but the 3% solution failed.

As a result of these incomprehensible results, we decided to develop an in-house testing capability. We set aside the space, obtained the necessary equipment, and trained personnel who would be handling the TB microorganism, which is moderately dangerous. We then began our investigation of the AOAC TB test.

During this period, Dr. Joseph Ascenzi, a SURGIKOS microbiologist, was appointed Associate Referee for the AOAC TB test; Dr. Reto Engler, Disinfectant Branch Chief at EPA, was designated as the AOAC General Referee. Dr. Engler directed Dr. Ascenzi to identify the shortcomings in the AOAC test method that caused inconsistent results to be obtained and to determine whether those shortcomings were correctable. Failing that, Dr. Ascenzi was to generate a scientifically sound test method.

By 1983, we had identified the following faults in the AOAC test:

1. The existing AOAC tuberculocidal method precludes any control over the starting population which has been found to be highly variable. The starting number of microorganisms in the population, used to challenge the disinfectant has a very significant effect on the time required to show complete kill by the disinfectant.

In addition, there is a pronounced tendency for microorganisms to be washed off the carriers into the disinfectant, thus effectively reducing the potential recovery of viable bacteria.

2. The mycobacteria used as the test organism is very sensitive to the temperature of disinfection which is frequently poorly controlled due to the use of biosafety hoods and other equipment used during the performance of this test.

Another factor which may be involved in the failure to recover low numbers of viable mycobacteria is the use of liquid recovery culture methods which are not optimum for culture of this organism. All of these deficiencies render the existing AOAC TB test inaccurate and not reproducible.

Moreover, all of the faults found in the AOAC TB test method tend to increase the likelihood of accepting a weak disinfectant but not of rejecting one which is, in fact, efficacious. The errors tend to be in the direction of greatest possible risk of failure to disinfect. The existing AOAC TB test was the best methodology available when it was introduced in 1968, but better methods have since been developed.

The development of a new quantitative TB test took place over a period of three years, using SURGIKOS laboratory personnel as well as contracted expertise at the Trudeau Institute, Saranac Lake, New York and the National Jewish Hospital, Denver, Colorado. The studies showed that the quantitative method is reproducible and that the test organisms are very representative of the pathogenic strains of M. tuberculosis causing illness in humans.

The new quantitative test method was presented to Dr. Engler in March of 1983. We reviewed the method with microbiologists of the EPA Disinfectants Branch that same month. At that meeting, considerable attention was focused on the problems inherent in the old method as outlined above.

Dr. Engler conveyed EPA's comments and recommendations to us in April. We reviewed and incorporated them into the new test method, and returned the modified document to the agency in August 1983.

The new test method continues in the standard AOAC approval process. The interlaboratory collaborative study will begin shortly. We anticipate that this process, which began in 1978 with the appointment of the Associate Referee, will require at least another year to complete. In the meantime, the existing inadequate AOAC TB test continues to be used.

Many of the problems which we have encountered during the development of the new quantitative TB test method might have been avoided had EPA's Beltsville Laboratory been in operation. The laboratory could have served as a focal point for evaluation of proposed test modifications rather than the existing and somewhat cumbersome AOAC procedure. Had this option been available to us, we believe that questions about the TB test method would have been resolved three years ago.

The reopening of the Beltsville Laboratory, in conjunction with a revised definition of hospital disinfectant, could make a significant contribution in the areas of verification of registration testing, enforcement activity, and improving the accuracy of disinfectant labeling as understood by users.

Conclusion

In conclusion, we believe that the regulatory process will be improved by:

1) the agency's use of the commonly accepted definition of hospital disinfectant, and

2) speeding the process by which EPA verifies and approves modifications to acceptable testing procedures.

Mr. Chairman, we wish to commend the Committee for identifying and shedding light on these problems.

Senator SARBANES. Thank you, Mr. McQuade. That was very helpful testimony.

Our final witness will be Mr. Ralph Engel, president of the Chemical Specialties Manufacturers Association. We are happy to have you here.

STATEMENT OF RALPH ENGEL, PRESIDENT, CHEMICAL SPECIALTIES MANUFACTURERS ASSOCIATION

Mr. ENGEL. As noted, I'm president of the Chemical Specialities Manufacturers Association, and I'm accompanied today by Mr. Harold Eitzen, on my left, who is an industrial hygienist, and laboratory director and chief executive officer of Micro Air, a most recently formed company. Prior to that time he was associate professor of pathology and director of the Department of Health Infection Control and Environmental Health Laboratory at the Indiana University Medical Center.

CSMA has a membership of some 400 firms engaged in the manufacture, formulation, distribution, and sale of antimicrobial products, as well as other chemical specialty products for household, institutional, and industrial use.

The association represents companies that formulate and market hard surface disinfectants used in hospitals and other facilities where a clean, aseptic environment is desired. All of these hard surface disinfectants must be registered by EPA, under the authority of FIFRA.

It is most important that we have a common understanding of the various types of antimicrobial products used in the health care environment, and I have heard them touched on by Mr. Rutala this morning. Let me just make further comment.

First, there are hard surface disinfectants, and these are products designed to reduce the number of pathogenic organisms to nonharzardous levels on hard surfaces such as floors, walls, and countertops. Please note that the function of hard surface disinfectants is not to completely sterilize a surface, but to keep microbial contamination at nonhazardous levels. These products are used as an added protection in routine cleaning and maintenance to improve facility hygiene.

Cold sterilants are a second class of hospital antimicrobial products subject to FIFRA. These products serve a very different purpose. They sterilize medical instruments used in or on the body, and are subject to different standards and testing procedures than hard surface disinfectants.

A final class of hospital-use antimicrobial products consists of topical antiseptics, presurgical hand scrubs, and other products designed to kill bacteria on the human body. These products are not registered by EPA under FIFRA, but are regulated by the U.S. FDA.

We are here today to address hard surface disinfectants, as this is the area of our expertise.

CSMA is in full support of S. 2659, which would amend section 3 of FIFRA to require EPA to establish efficacy standards for antimicrobial products used to control microorganisms of human health concern. The Agency would also be required to monitor these products and bring enforcement actions when products clearly fail to meet these standards.

Hard surface disinfectants are currently subject to such compliance monitoring through testing conducted under EPA grants in the laboratories of at least four States: Florida, North Carolina, Virginia, and Mississippi. We believe, however, that a single, federally operated disinfectant efficacy testing laboratory would provide the best means of assuring that all disinfectants are effective when used according to label directions. And we believe that for this laboratory to best serve the public, we must have efficacy standards that are based on sound statistical and microbiological principles. We hope that this is the goal and intent behind S. 2659.

Although CSMA supports the bill, we do disagree with some of the statements made in its support. Those statements would indicate that many or most or a lot of disinfectants do not work. Considering that the role of hard surface disinfectants in hospitals and other health care facilities is to assist in limiting the numbers of pathogenic organisms to nonhazardous levels on hard surfaces such as floors, walls, and countertops, those comments are not well founded.

Disinfectants serve as a valuable addition to routine cleaning and the maintenance of a reasonably aseptic environment. We firmly believe that hospital-use disinfectants currently marketed by CSMA members are very effective for this purpose when used according to label directions. We know of no validated instances where the use of current hard surface disinfectants, used according to label instructions, has led to cross infection in hospitals.

The primary reason for our support of S. 2659, and for a single national facility for monitoring disinfectants, is related to the tests that are currently used to measure the efficacy of disinfectants, especially the AOAC use-dilution test. That, incidentally, is a different test procedure than one conducted for tuberculocidal testing.

This test is subject to significant variation in results, and thus requires a very, very high degree of expertise to perform properly and consistently. It has become a common experience in our industry for an antimicrobial product to pass the test in one State and fail in another. This has become a significant problem for our members in recent years. We believe this problem would be greatly attenuated, if not cured, by having this testing performed in a single laboratory.

CSMA has long recognized that improving the repeatability of the use-dilution test will require a concerted scientific effort, and this effort is well on its way. We began discussions with EPA in early 1982 on this issue, and we helped to establish a broad-based formal effort through the Association of Official Analytical Chemists, or AOAC, in 1983.

The primary goal of this effort has been to modify and further define the procedures of the use-dilution test so that results will be more consistent. We have made significant efforts to work with EPA to develop better criteria based on this test; criteria which take into account the inherent statistical variabilities in the results of a biological test.

Let me summarize the views of our industry.

CSMA supports the reopening of the Federal testing laboratory as an alternative to the increasing number of State or other private testing facilities.

CSMA scientists will continue to work through AOAC, and with government and academia, to improve the reproductibility of the use-dilution tests for disinfectant efficacy.

We remain ready to work with EPA to revise, as needed, the criteria for disinfectants based on sound statistical and microbiological principles to bring the criteria within the reproductibility limitations of the use-dilution test.

And most importantly, CSMA and the disinfectants industry remain committed to producing safe and effective disinfectant products.

Now, Mr. Chairman, I would like, if I may, to introduce Mr. Eitzen, who will provide you with a brief but further review of the scientific aspects of this issue, if he could.

Senator **SARBANES**. I certainly will be happy to hear from you, Mr. Eitzen.

STATEMENT OF HAROLD E. EITZEN, PH.D., LABORATORY DIRECTOR AND CHIEF EXECUTIVE OFFICER, MICRO AIR, INC.

Mr. **EITZEN**. Mr. Chairman, Senator Gore. I am Mr. Eitzen, from Indianapolis, Indiana. As a hospital epidemiologist, I am actively involved with the efforts of CSMA and its member companies to address the issue of disinfectant efficacy test methods and standards.

The AOAC use-dilution test is the primary test used to evaluate the efficacy of hard surface disinfectants. In this test procedure, small metal cylinders are dipped into a suspension containing a standard test organism, coating the cylinder. After drying, the cylinders are placed for 10 minutes in tubes containing the recommended end-use dilution of the disinfectant being evaluated. Each cylinder is then carefully drained of disinfectant and placed in a tube of disinfectant neutralizer. If any living organisms remain on the surface of the cylinder, regrowth of the organism will be observed.

The test, therefore, provides a measure of the probability of an individual cylinder being made completely free of bacteria by the disinfectant. If even one organism survives, regrowth will occur, and the cylinder will be found not to be sterilized.

This standard of complete sterilization is part of the challenge we face in interpreting the results of the use-dilution test. Remember, the purpose of a hard surface disinfectant is to limit microbial contamination to nonhazardous levels.

The basic use-dilution tests have been used to evaluate efficacy for more than 20 years. There have been several modifications and additions to the tests over the years which were based on regulatory judgment, and have not been validated through collaborative scientific and statistical study. These major changes include an increase in the number of cylinders used in the test, the addition of hard water to support hard water label claims, the addition of blood serum to evaluate one-step cleaning and disinfecting, and the addition of a more difficult-to-kill microorganism, Pseudomonas aeruginosa, for hospital-use products.

As Mr. Engel has said, CSMA has started its efforts to improving these tests in 1982 and worked to establish an ongoing broad-based scientific artery with the AOAC in 1983. We believe we are making significant progress. We have conducted a number of laboratory investigations leading to a recently completed collaborative study to assess the variability of the basic tests from laboratory to laboratory.

To understand the scientific problems to overcome in setting and enforcement standards based on the use-dilution test, it is important to understand why the results may vary. There are two primary reasons.

First, any laboratory evaluation procedure, especially one based on living biological organisms, is subject to interlaboratory and day-to-day variability due to test materials, conditions and procedures not being perfectly standardized. For example, the organisms may have different resistances due to slight variations in growth conditions. Some metal cylinders may harbor bacteria in pits and scratches where they are not exposed to disinfectants. Also, operator techniques may vary. These and other variables affect the probability of each cylinder being completely disinfected in a given test. Our efforts at the AOAC have been aimed at controlling and identifying these and other variables to the extent that this is possible.

The second source of the variability is statistical in nature. There is an inherent statistical uncertainty in the results of a test such as the AOAC use-dilution test that cannot be reduced through more careful standardization of organisms, equipment, and techniques. Remember that what we are trying to measure with the test is the probability of each cylinder being completely disinfected.

To provide a basis to assess and take into account this latter type of statistical uncertainty as it applies to the use-dilution test for disinfectants, CMSA has sponsored two important studies by an independent university statistician. The first of these was published in the July 1985 Journal of the Association of Official Analytical Chemists. It presents for the first time the basic statistical concepts needed to understand the test and demonstrates the stringency of the current registration criteria.

The second paper is now scheduled for publication in the same journal. It goes further to provide a historical perspective on how these criteria developed, and provides a more appropriate alternative registration procedure based on well-accepted dose-response statistics.

CSMA funded these two evaluations because we believe that an accurate statistical framework is very essential to the development of better efficacy standards in compliance monitoring. We believe the current efforts will result in the development of better standards for disinfectants, standards that are based on sound scientific and statistical principles, standards that can be monitored and enforced.

The science of antimicrobial efficacy evaluation is not static, and our understanding of the complete biological and statistical variables involved in the use-dilution test is continuing to increase. The disinfectants industry remains firm in its desire to produce products that are both safe and efficacious. CSMA and its member companies will continue to work cooperatively to improve test procedures and standards needed for the effective registration monitoring and enforcement of their products.

Mr. ENGEL. Mr. Chairman, we greatly appreciate the opportunity to appear before your committee and yourself to voice our support for S. 2659 and to explain some of the problems associated with the current efficacy standards for hard surface disinfectants. Mr. Eitzen and I will remain to respond to questions where we can. Thank you very much

Senator SARBANES. Thank you, Mr. Engel, and I thank all the panel.

Mr. Eitzen, I have just one question. I want to make sure I understand one point. In your statement you refer to the addition of hard water to support hard-water label claims that were made in the use-dilution test—what exactly does that mean?

Mr. EITZEN. Water varies, of course, across the country. In some areas municipalities or regions may have water that is significantly harder than other areas. It has more minerals in it. And this usually cuts down the efficacy of a disinfectant. So, hard water was then added to the test to determine whether or not certain disinfectants, if they claim hard-water effectiveness, really are.

Senator SARBANES. So, if the label made a claim of hard-water effectiveness then they required hard-water testing?

Mr. EITZEN. That's true.

Senator SARBANES. Was it your view that such a test was not validated through collaborative and scientific statistical study?

Mr. EITZEN. That's right. It hasn't been collaborated. It's probably not a bad idea to do such a test but it should be studied and collaborated on by scientific groups.

Senator SARBANES. I wasn't clear whether you were taking issue with that having been done or whether you thought it was appropriate to do that testing. If the label makes a hard-water claim, is it appropriate in the testing to use hard water?

Mr. ENGEL. Excuse me. Maybe I can do this on a nontechnical basis, if you would.

There was an AOAC test method developed and certain test procedures were added to it prior to the collaborative studies to see whether those test procedures were appropriate or not. Those collaborative studies were not done up front, but by fiat, principally by the regulatory agency, the hard-water claim was added to the AOAC test methods and have been conducted as a result.

Senator SARBANES. I see. So it's a matter of process, a point of process you are making?

Mr. ENGEL. Yes.

Senator SARBANES. It may in fact be appropriate but you think the study should have supported it.

Mr. ENGEL. Yes.

Senator SARBANES. All right.

Ms. Rhodes, let me ask you this question: As you do testing and screen products, do you encounter the following argument: This product is being used everywhere else, why can't we use it here in Florida as well? In other words, do you find yourself up against what's happening in the rest of the country, since you are one of the few States with a testing program?

Ms. **Rhodes**. Yes, sir. It's a very frequent argument. Likewise it's also a very frequent argument that the method is invalid for application because it has all these drawbacks, so you should not be having a regulatory program once the products are on the market. But, if you look closely at our statistics, and if we were to give you statistics for individual companies, there are numerous companies that we have never found ineffective samples—on a very rare, rare basis. Likewise, there are other companies that consistently we find within the State of Florida, North Carolina, Virginia, and EPA, consistently find to be ineffective by this particular procedure. And we try to be very careful to validate each other's results.

Senator **Sarbanes**. I would like to ask all of the panel this question. If we were to reestablish a national lab and national testing, would you expect the national test standard to be higher and more rigorous than may currently exist at the State levels? Or is generally applied in the industry?

Mr. **Shaffer**. I think so.

Senator **Sarbanes**. Why don't you use the microphone, Mr. Shaffer.

Mr. **Shaffer**. I think those tests could be made a little more stiffer. Things are changing. One thing that's never discussed here, I was in the division of antibiotics for 20 years before I went into this work, and one problem that's never come up are these antibiotic-resistant organisms. Those are tough things to kill. They are allergic—I mean they are resistant to all the antibiotics, but I don't know—someone suggested here something about having tests based on that. The problem right there is, how do you propagate an antibiotic resistant organism? That is very difficult. We tried that when I was at the Food and Drug and the organism would die if you don't have the proper drugs in there. You just can't propagate them so you can't make any test. Something has never been done.

I don't know what these acquired organisms are doing. Are they more sensitive to our disinfectants or not? No one has ever addressed that. I think that's what is being circulated around in the hospitals, and that's the organism the people get and that's the one that is making them sick. There's no defense against that. I don't know—it's a completely different area of responsibility there. I don't know what you can do about it. That's there.

Senator **Sarbanes**. Does anyone else want to respond to the question? What would you anticipate the standard of testing to be if testing were resumed in a national lab?

Mr. **McQuade**. Senator, as I metioned in my opening comments, I believe that one of the major steps that would achieve improvement of disinfectant labeling and would improve enforcement activity on a national basis would be the revitalization, if you will, of the standards used by the agency. I think one of the things the industry looks at when you develop a product, you go to the user and determine what the users' needs are and what would impact the user—the user brings to the product.

I think, while it was well recognized at the time the AOAC test methods were developed in the 1950's that they were the best available methods, I think we've made significant scientific advances which should be incorporated into new test methods. Again, I reemphasize the extreme need to improve, if you will, the definition that's used by the Agency, because, Senator, a disinfectant is a disinfectant and that's what the user understands. It kills everything except spores—whether it's used on the floor or on a cystoscope, it's still a disinfectant.

Senator Sarbanes. Okay.

Mr. Engel. Mr. Chairman, I think perhaps the standards will be simpler. But I think the fact that it is centered in one laboratory where the expertise can be centered will increase the efficacy of the products and the testing procedures, relative to those products. That's important.

Senator Sarbanes. I have sensed that industry often regards regulation as just a burden, an oppression, but that in this instance, proper regulation and proper testing could in fact help industry rather than hurt it. And I think in particular that it would contribute to sorting out within the industry the many manufacturers who are trying very hard to meet proper standards and the few who are ignoring standards in order to reap some short-term benefit. Do you have that perception?

Mr. Engel. Back in 1982 when we entered the issue, and thus agreed to represent the industry, the chairman of the board of CSMA noted to the industry that we would not defend those who would put out substandard products. Our industry is committed to develop the best products we can.

Senator Sarbanes. Senator Gore.

Senator Gore. Yes, Mr. Chairman, a few brief questions. I would like to follow through on the excellent line of questions you began on how we can imporve the testing standards as the program is reestablished, hopefully. I hope it can be. We'll certainly work together toward that end.

As I understand one of your—your next to the last response, Mr. Engel, while the current test is sorely deficient in many respects and one of its deficiencies is a tendency to produce inconsistent results depending upon who conducts the test, that when you have a centralized testing facility that has a high volume and consistent procedures for implementing the test, the reliability of the test improves significantly. Is that correct?

Mr. Engel. Because the personnel who would be conducting that test develop a high level of expertise and can interpret the test results and view the materials that they are using with the test.

Senator Gore. Very good. And nobody disagrees with that, I take it. However, while this would partially solve the problem of inconsistent results and improve the reliability of the current test, it would not address the kind of problem that Mr. Shaffer referred to and that Dr. Schaffner referred to on the first panel, and that is that the current test really measures only efficacy against three vegetative bacteria; correct? And, as Mr. Shaffer just pointed out and others have pointed out, the threat with which hospitals are confronted is far more complicated than the threats measured by these three vegetative bacteria. And it would be extremely helpful to hospitals and health care professionals if a better test could be designed which was predictive of the disinfectant's ability to deal with these other kinds of bacteria that pose a more significant problem in hospitals; is that fair to say? Does anybody disagree with that?

Mr. Engel. Senator, we don't disagree but we ask you to keep in mind that there are generally three types of disinfectant products, used differently, having different purposes. They do not do the same job.

Senator Gore. I understand. You are sort of looking down into the future and you are seeing the possibility of a very, very stringent test that might be more stringent than these hard surface things really need to——

Mr. Engel. That nobody would pass.

Senator Gore. That's certainly to be kept in mind. At the same time, if we are going to devote all of this attention to this problem, which is a big problem, we might as well do it right and in seeking to reestablish it, as the chairman indicates, we ought to try to improve the test. Can that be done? Can we get a test of the kind that's predictive against the threats that you are more concerned about?

Mr. Eitzen. Senator Gore, there are avenues right now to do additional testing as needed on disinfectants. For example, there are not many hospitals today that house tuberculosis patients. If there are some that do have particular wards, have these kinds of patients cared for, and disinfectant companies are going to make claims, if they have claims on their label for tuberculocidal effectiveness, then there is a test that can be used to determine whether the product is effective or not.

So, depending on what is needed——

Senator Gore. So you'd have organism-specific tests that can be used to supplement the current test in specific instances. But we are talking about something a little better and broader in scope than that. At least that's what I'm asking about, whether or not it is possible.

Ms. Rhodes.

Ms. Rhodes. Well, Senator Gore, I think it's definitely possible and definitely desirable but it's also a very long-term process. This is what we began about 3 years ago with a task force, along with the Association of Official Analytical Chemists, to specifically look at this test procedure that is used currently for registration and enforcement and to revise it, improve it, and to make it less variable. It has been a long-term process. It is nowhere near completion. I think it's very desirable and it's advisable but it's not going to be a very quick item to accomplish.

Senator Gore. Do you have a report that might be useful to us on that particular point?

Ms. Rhodes. Yes. We'd be more than happy to furnish that. The only place I somewhat disagree with Mr. Engel's comments is relative to the fact of the variability of enforement testing currently being done. I would disagree there. Because I do not feel that there is disagreement in the enforcement testing between Virginia, North Carolina, and EPA verification of all those three States currently. But we rightly support the need for a Federal program, not only to validate some of the registration data but to continue to help verify State's data, and to act as the primary enforcement agency.

Senator GORE. Now, I want to make this point here. Any complaints about the test that was used to monitor the efficacy of these disinfectants applies, also, to the test for registering and getting the permit or license to sell these things in the first place. So, if the test—if there are shortcomings in the test for monitoring, then there are shortcomings for getting on the market in the first place. That's another argument for not only reestablishing the testing program but improving the standards in the process.

Mr. McQuade, you wanted to respond.

Mr. MCQUADE. Senator, if I may try to strike kind of to the heart of the matter, at present there are several tests that can be done by the manufacturer of a broad-spectrum disinfectant. They include the use-dilution test, for germicidal, fungicidal, tuberculocidal, and virucidal claims. The problem is we have to reeducate the user of these products or we have to change the definition of the word "disinfectant," because in a hospital setting, in an emergency room, in a large metropolitan area, if you have an indigent person who has been severely injured by an automobile accident, for example, how is it possible to detect what organisms this person might be carrying? And if the hospital community, the health care practitioner, has been raised through his schooling to believe the definition of a disinfectant is that it inactivates all microorganisms except spores, why is he now supposed to read a label to see of it's active against TB, is it active against eipophillic viruses. The definition is the crux of the situation we are facing right now.

If you fix the definition and if we utilize words such as sanitizer, bacteriostat, we can categorize all of the products that exist today and, in fact, the Agency in its guidelines had definitions that can be apropos to these other products.

But, when you talk to me, sir, about a disinfectant, my understanding from my school days is it kills everything but spores. And that's what our users expect and that is where the first deficiency exists. We need to repair the definition used by the Agency.

Second, we need to look at the existing test methods. As I mentioned before, the majority were developed in the mid to late 1950's, early 1970's. We have made many scientific advances that can be brought to bear on this problem.

Senator GORE. I think the important point is that every member of the panel supports the legislation. Even the industry—perhaps particularly the industry supports reestablishment of this testing program. I certainly support that.

I'm going to finish just in a brief moment. You say in your statement, Mr. Engel, you separate hard-surface disinfectants from the disinfectants that are used on medical instruments. And you say—you are only speaking in behalf of the hard-surface disinfectant industry so when you say you don't think there's a validated study tracing a cross infection to hard surface, you would not make the statement that there are no validated instances where the use of disinfectants——

Mr. ENGEL. No, sir, I would not. But I think Mr. Eitzen can lend some help. He talked to me last night about hospitals and infection rates——

Senator GORE. I just wanted to get to that. If you want a brief addition, I want it. Go ahead.

Mr. EITZEN. Well, we agree, certainly we agree on getting our laboratory back, doing the testing. We do not want it implied that all of these nosocomial infections that we have been talking about all day are caused by or aided by hard-surface disinfectants.

Senator GORE. I said in my statement that even if all of them work perfectly and all of them were applied exactly perfectly, there would still be hospital-caused infections. You know, I think that ought to be clear.

At the same time, there are numerous instances in the literature of disinfectants, the kind used to sterilize medical instruments, primarily, that have caused outbreaks of infections. And common sense tells us that that's only the tip of the iceberg because most such cases are not going to be tracked down and reported.

Well, I think that this has been an extremely valuable hearing and I just want to say, in closing my part of it, Mr. Chairman, again, how much I appreciate your willingness to have this hearing and your long-term concern about the issue. I look forward to working with you to follow through on this hearing and get something done about it. I would also like to thank all of the witnesses on this panel, and previous panel. I have been to very few hearings where the witness list was of such uniform high quality and sustained focus on the heart of the problem that we are addressing here. I just wanted to express my thanks to everyone who participated.

Senator SARBANES. I want to echo our thanks to the panel. You have been enormously helpful to the committee. We appreciate it very much. The hearing stands adjourned.

[Whereupon, at 12:20 p.m., the subcommittee adjourned, subject to the call of the Chair.]

DECLINING FEDERAL HEALTH AND SAFETY STANDARDS: HOSPITAL DISINFECTANTS AND ANTISEPTICS

THURSDAY, SEPTEMBER 25, 1986

Congress of the United States,
Subcommittee on Investment, Jobs, and Prices
of the Joint Economic Committee,
Washington, DC.

The subcommittee met, pursuant to notice, at 9:40 a.m., in room SD-628, Dirksen Senate Office Building, Hon. Paul S. Sarbanes (member of the subcommittee) presiding.

Present: Senators Sarbanes and Gore; and Representative Fiedler.

Also present: William Buechner, professional staff member.

OPENING STATEMENT OF SENATOR SARBANES, PRESIDING

Senator Sarbanes. The subcommittee will come to order.

Of course, these are the closing days of the session and we expect some floor activity in about an hour's time, so we will try to move expeditiously here with the hearing and with the opportunity to question the witnesses.

This is the fifth in a series of hearings which the Subcommittee on Investment, Jobs, and Prices of the Joint Economic Committee has been holding on the current state of Federal health and safety standards in areas of immediate concern to Americans and the social and economic ramifications of lowering those standards.

Today's hearing continues the inquiry begun in the hearing of the 7th of August into hospital disinfectants and will focus as well on the closely related question of antiseptics.

Earlier hearings in this series focused on a range of problems, including air transportation, fire prevention and control, and child health. Our testimony received in the course of those hearings consistently and regrettably underscored the growing concern in the Congress, in the media and in the public at large that Federal health and safety programs have been eroded and that the cause of the erosion lies in irresponsible budget cuts, in some instances in sweeping arbitrary deregulation, and often in the complex interaction of the two.

Particularly disturbing is what appears to be a well-defined trend described in a 1984 study conducted by former EPA Deputy Administrator William Drayton. In Administrator Drayton's words:

> The trend is not the work of any one manager. It is a governmentwide pattern with a resulting protection gap potentially enormous in scale.

When we consider that some 34 million Americans will be hospitalized this year, the effectiveness and dependability of hospital disinfectants and antiseptics must be a matter of serious concern. At present there is no standard system for determining their reliability. The situation is further complicated by a division of authority since the EPA is responsible for overseeing disinfectants and the FDA is responsible for overseeing antiseptics.

The August 7 hearing to which I referred earlier focused exclusively on disinfectants. These products must be registered by the Environmental Protection Agency in accordance with EPA standards. But the EPA relies on manufacturers' assurances that the standards are indeed met since it has no independent means of verification.

This was, of course, not the case prior to 1982. Until that time, the Federal Government had maintained independent testing facilities in the Department of Agriculture which were simply transferred to the EPA when the latter Agency was established.

Expert witnesses on August 7 drawn from several of the Nation's major schools of medicine and public health, from the industry, and from one of only four States which has undertaken its own testing program, all agreed that regularized testing procedures to assure reliability is essential and that this can be done most effectively and efficiently at the Federal level.

They were unanimous in their view that the 1982 decision of the administration to close its EPA testing facility and thereby abandon Federal responsibility in this area, a decision justified on the grounds that it reflected the administration's general policy of deregulation and that it would reduce EPA costs, was a short-sighted and ill-advised decision.

The situation is even more haphazard, if one can use that term, with respect to FDA review of antiseptics. While the EPA has no independent means of verifying manufacturers's assurances of reliability, it has nonetheless established formal standards of reliability.

The FDA, in contrast, has no such registration standards. A tentative final order was published in January 1978 but was never officially adopted, can be ignored by manufacturers if they so choose, and has been overtaken by developments in the field since that time.

The U.S. Public Health Service estimates that secondary hospital-based nosocomial infections annually cause 20,000 deaths, contribute to an additional 60,000, and represent an additional $2.5 billion in health care costs.

It is with these sobering statistics and the August 7 testimony in mind that the subcommittee today seeks to elicit comment from the two agencies with direct responsibility—the Environmental Protection Agency with respect to disinfectants, and the Food and Drug Administration with respect to antiseptics.

We have with us this morning representing the agencies Douglas Campt, Director of the Office of Pesticide Programs, Office of Pesticides and Toxic Substances of the EPA; and Dr. Peter Rheinstein of the Office of Drug Standards of the Center for Drugs and Biologics of the Food and Drug Administration.

Gentlemen, we are ready to hear from you. Mr. Campt, perhaps we'll take your testimony first and then turn to Dr. Rheinstein.

STATEMENT OF DOUGLAS D. CAMPT, DIRECTOR, OFFICE OF PESTICIDE PROGRAMS, OFFICE OF PESTICIDES AND TOXIC SUBSTANCES, U.S. ENVIRONMENTAL PROTECTION AGENCY

Mr. **Campt**. Good morning, Mr. Chairman. I appreciate the opportunity to discuss with you this morning antimicrobial products, particularly disinfectants, sanitizers, germicides, and sterilizers.

Senator **Sarbanes**. Let me say your entire statement will be included as submitted in the record. This will apply also to you, Dr. Rheinstein, in case you wish to abridge it or move away from it at some point.

Mr. **Campt**. Yes, I will summarize.

Senate bill 2659 has as its goal the same results we all want—to make sure disinfectants work. However, we cannot support the implementation of a comprehensive monitoring and enforcement program based on Federal testing. There are other better approaches than routine testing of all antimicrobials by the Federal Government. We must seek ways to make registrants more accountable for the efficacy of their products.

The Office of Pesticide Programs has begun to place greater emphasis on the disinfectants program with the goal being more effective approaches to the regulation of antimicrobials. With that in mind, the Agency has identified five primary objectives which we believe are necessary for a successful program. These are:

No. 1, reproducible efficacy tests. Tests of the same material should yield the same results over and over.

No. 2, predictive value. We must make sure that the test itself is a meaningful surrogate for assessing the performance of the product in the real world.

No. 3, quality control. People should have meaningful assurance that the product they are about to use is of the same quality as the material which passed EPA's efficacy tests.

No. 4, prevention of toxic effects. People who may be exposed to antimicrobial products must not be subjected to untoward health effects from exposure to antimicrobial products.

No. 5, accurate labeling and advertising. Protecting people from the consequences of unsupported product claims requires a strict policy on labeling and advertising and a willingness to enforce it.

To do a more thorough job, the Agency must solicit the participation from outside experts, the manufacturing community, the Association of Official Analytical Chemists (AOAC), the FIFRA Scientific Advisory Panel, FDA, CDC, and others. The Agency must evaluate data bases and require the submission of additional data, evaluate those data, and determine how best to avoid risks when they are found.

To carry out this five-point program, the Agency is developing a strategy to integrate all phases of the program and to implement improvements.

That strategy includes: First, reproducible efficacy tests. Disinfectants are a pesticide category for which efficacy data are required. The target pests are invisible to the naked eye, such as bacteria, fungi, and viruses. Therefore, we need a means of ensuring the product efficacy since the consequences of failure can be significant. The AOAC use-dilution test has been the subject of considerable criticism in the past decade because of alleged poor reproducibility. Consequently, in 1983, the Agency committed to a formal standardization and update of this test.

EPA has taken the lead in this effort by entering into a cooperative agreement with Mr. William Rutala of the University of North Carolina's School of Medicine. The ultimate plan is to design and produce a test method which is as concise and unambiguous as is practicable so there is a minimum of interlaboratory variation in methods of results.

The final series of collaborative studies is underway and will be completed in December of this year. We anticipate a final report with recommendations for a test protocol early in the spring.

The second is predictive value. Tests must be meaningful and must be a representative assessment of efficacy when the product is used as directed.

A second AOAC testing protocol, the AOAC tuberculocidal activity method, has also been the subject of some criticism, both because of reproducibility problems and because of questions of predictability. After a thorough evaluation of the problem, the Agency published a new regulatory policy last May. The new policy allows applicants for registration to chose from three testing options.

The new policy applies to holders of existing registrations as well as applicants for new registrations, and it includes provisions for verification of the validity of suspect efficacy claims and for demonstrating reuse capacity.

Third, quality control. The public must have a meaningful assurance that each pesticide lot does indeed meet EPA requirements. Antimicrobials have been regulated, to some extent, since 1912. Congress clearly placed the burden of proof on registrants to show that a registered pesticide is effective. The Agency requires applicants for registration to submit efficacy data specific to each product that bears a claim to control organisms which may pose a threat to human health, either directly or through transmittal of disease.

In the past, the Agency conducted a token amount of efficacy testing at the Beltsville laboratory. This testing was extremely limited. The Agency's postregistration testing for the 16-year period prior to 1982 showed a failure rate of about 15 to 16 percent. The majority of the products tested were selected for testing because of earlier failures.

The testing of antimicrobial products at the Beltsville lab was phased out in 1982 for several reasons.

No. 1, the efficacy testing at Beltsville was inadequate. The Federal Government merely conducted a few screening tests.

No. 2, the Agency recognized a serious need to update the methods. Without a reliable test method, the value of any monitoring or enforcement program is greatly diminished. More time and effort could be directed toward the evaluation and improvement of test methods.

No. 3, it became apparent that the Beltsville laboratory was creating a false sense of security among users and in the public generally. During the last 10 years of the program, of the tens of thousands of batches of the roughly 20,000 antimicrobial products that are registered, the number of samples averaged about 125 per year.

The Agency's decision to discontinue the Beltsville program in 1982 should not be construed as an abandonment of EPA's strong commitment to public health protection. Rather, the issue is a question of how such protection can be achieved most effectively and in the most cost-effective manner.

The Agency is considering whether it can require the registrant to conduct efficacy testing on a lot-by-lot basis through regulation, or whether the Agency could require the registrant to employ a third party laboratory to conduct verification testing.

Going on to prevention of toxic effects, FIFRA requires a finding that the use of a pesticide will not result in unreasonable adverse effects on people or the environment.

The Agency has been looking at the quality of the data bases for antimicrobial pesticides. As I mentioned earlier, antimicrobials give rise to particular concern about their efficacy, but the need for efficacy data should not overshadow the necessity of adequate exposure and toxicity data. In 1985, we established a work group to review the Agency's policies regarding toxicology data. The work group concluded that a tiered testing system should be implemented. The system would first require a minimal level of toxicology data and exposure data for all products, and if a product met certain criteria a second tier of studies would be required, and so on. We anticipate issuing letters by the end of this year requiring all registrants to submit appropriate data pursuant to section 3(c)(2)(B).

Accurate labeling and advertising. Finally, to protect the public from relying on false claims of efficacy by disinfectant manufacturers, it is important to have strict controls on labeling and advertising. The Agency recently reconsidered its policy with respect to antimicrobials. Efficacy claims that are not supported by efficacy data may foster a false sense of security among health professionals relying on the use of that product. In order to protect public health, the Agency decided that a new policy was necessary for antimicrobial products.

The new policy prohibits anyone with a financial interest in one of these products from making any claims for it which differ from those on the EPA-approved labeling. EPA's Office of Compliance Monitoring has sent notices to each company reported to be making such claims. Thus far the results have been good, but the Agency has made it clear that any future violations will be met with strict enforcement measures.

In conclusion, the Agency is working to improve the disinfectants program and progress is being made. We anticipate having a new strategy ready around the first of the year. In the meantime, we have ongoing activities which will continue. We have one test method in place and will soon be ready to implement improvements in the use-dilution test. We have reevaluated our toxicity data requirements. We have notified registrants of tuberculocides of new efficacy data requirements and we have cracked down on possibly misleading advertising. We are looking for and evaluating new approaches to improve the program, but we are taking steps now to make this a strong regulatory program with aggressive oversight.

Mr. Chairman, I would be happy to answer any questions you may have.

[The prepared statement of Mr. Campt follows:]

PREPARED STATEMENT OF DOUGLAS D. CAMPT

Good morning Mr. Chairman and members of the Subcommittee. I appreciate the opportunity to discuss with you this morning antimicrobial products, particularly disinfectants, sanitizers, germicides, and sterilizers. These products constitute an important category of pesticides regulated by the Environmental Protection Agency.

Senate bill S. 2659, which Senator Gore introduced has as its goal the same result we all want--to make sure disinfectants work. We want health professionals and the public in general to be able to use disinfectants and other antimicrobials with confidence that they will do exactly what is expected of them. However, we cannot support the implementation of a comprehensive monitoring and enforcement program based on federal testing. There are other better approaches than routine testing of all antimicrobials by the federal government which can provide a significant measure of assurance. We already have efficacy standards for disinfectants and other antimicrobial products, but we must seek ways to make registrants more accountable for the efficacy of their products. It makes more sense to improve efficacy testing protocols; to ensure that all antimicrobial products (old and new) meet current testing requirements; and to cancel or suspend registrations of those which do not meet EPA standards. It is my belief that responsible producers will welcome such measures.

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), section 3(c)(5) provides that a pesticide product shall be registered if (A) its composition is such as to warrant the proposed claims for it; (B) its labeling and other required submissions comply with the requirements of FIFRA; (C) it will perform its intended function without unreasonable adverse effects on the environment; and (D) when used in accordance with widespread and commonly recognized practice, it will not generally cause unreasonable adverse effects on the environment. That subsection also provides that the Agency may waive efficacy data requirements. The Agency has waived the requirement of submission of efficacy data for many pesticides, but because of the potential for serious public health consequences and the inability of users to discern the effectiveness of antimicrobial pesticides, the waiver specifically does not apply to public health-related antimicrobials such as hospital disinfectants. The Office of Pesticide Programs has begun to place greater emphasis on the disinfectants program with the goal being more effective approaches to the regulation of antimicrobials. With that in mind, the Agency has identified five primary objectives which we believe are necessary for a successful program.

1. REPRODUCIBLE EFFICACY TESTS

   When testing the efficacy of a product, tests of the same material should yield the same results over and over, regardless of where the test is conducted or by whom.

2. PREDICTIVE VALUE

   It is not good enough to simply develop a test which gives consistent and reproducible results in the laboratory. To meet public health goals, we must also make sure that the test itself is a meaningful surrogate for assessing the performance of the product in the real world. We want to know that a product which has passed EPA's test will actually kill bacteria and viruses when it is used to wash the operating table.

3. QUALITY CONTROL

   People purchasing and using an antimicrobial pesticide should have meaningful assurance that the product they are about to use is of the same quality as the material which passed EPA's efficacy tests.

4. PREVENTION OF TOXIC EFFECTS

   Users and other people who may be exposed to antimicrobial products must not be subjected to untoward health effects from exposure to antimicrobial products.

5. ACCURATE LABELING AND ADVERTISING

   The public must be able to rely on representations of efficacy found on product labels and in advertising.

Protecting people from the consequences of unsupported product claims requires a strict policy on labeling and advertising and a willingness to enforce it.

Development of reproducible test protocols which have predictive value takes years to accomplish. To do a thorough job, the Agency must solicit the participation of outside experts. Input from the manufacturing community will always be available because it is their business, but we also need input from other sectors, such as the Association of Official Analytical Chemists (AOAC), other government agencies, public and private institutions, and users of disinfectants. In the past the Agency has solicited the assistance of the FIFRA Scientific Advisory Panel which is composed of eminent scientists from outside the government. We intend to continue to seek that body's advice and assistance whenever we are in need of its technical expertise. The Agency also participates in an Interagency committee made up of FDA, CDC, and EPA. That group has been involved in efforts to promote a unified approach to such matters such as antimicrobial regulation, which affect all three agencies. In order to protect people from adverse health effects from exposure to toxic antimicrobial products, the Agency must evaluate data bases, require the submission of additional data, evaluate those data, and determine how best to avoid risks when they are found. This is a long, labor intensive, and costly undertaking.

To carry out this 5-point program, the Agency will develop a strategy to integrate all phases of the program and to implement improvements. We expect to be ready to share that strategy with experts in the field around the turn of the year. Meanwhile the Agency is not sitting still. Several activities are well underway.

REPRODUCIBLE EFFICACY TESTS

Disinfectants are a pesticide category for which efficacy data are required and assessed as a condition of registration. The user cannot see whether a disinfectant is working, since the target pests are invisible to the unaided eye--such as bacteria, fungi, and viruses. We need a means of ensuring the product efficacy since the consequences of failure can be significant, even mortal. Laboratory tests are used to predict the efficacy of antimicrobial products to kill or control the target organisms. One of the primary vehicles for assessing disinfectant efficacy is the AOAC Use Dilution Test (UDT), a standard protocol for testing antimicrobial pesticides prescribed by the AOAC. The AOAC Use Dilution Test has been the subject of considerable criticism in the past decade because of alleged poor reproducibility. Two different labs testing the same product using the same AOAC test procedure reportedly often obtain different results.

Seventeen variables which theoretically could affect test results were identified by laboratory workers in industry, commercial, federal, and state laboratories. Industry has suggested that these variables produce inconsistent results from laboratory to laboratory. Consequently, in 1983 the Agency commited to a formal standardization and update of the Use Dilution Test. EPA agreed to participate actively in the AOAC/Industry Task Group convened to accomplish this task. Since then EPA has taken the lead in this effort by entering into a cooperative agreement with Dr. William A. Rutala of the University of North Carolina's School of Medicine, an expert in the fields of infection control and microbiology. This agreement provides for statistical analyses and laboratory support to update the test. The ultimate plan is to design and produce a test method which is as concise and unambiguous as is practicable so there is a minimum of inter-laboratory variation in methods or results.

The final series of collaborative studies is currently underway and will be complete in December of this year. We anticipate a final report with recommendations for a test protocol early next spring.

PREDICTIVE VALUE

Development of a test which is reproducible is only the first step; at the same time, tests must be a meaningful and representative assessment of efficacy when the product is used as directed. For example, it is important to know that a tuberculocidal product will actually protect people from TB. Also, we currently have no disinfectant product approved for use against the AIDS virus. (Only sterilization methods are currently approvable.) Until the Agency has a test protocol which will reliably predict that a product is effective in killing the virus, EPA cannot approve claims for that use.

A second AOAC testing protocol, the AOAC Tuberculocidal Activity Method, has also been the subject of criticism, both because of reproducibility problems and because of questions of predictibility. The Agency had been advised by several sources, including registrants, testing laboratories, researchers, and other scientific groups, that a generic efficacy problem existed with regard to disinfectants (particularly gluteraldehyde-based products) and their tuberculocidal effectiveness. After a thorough evaluation of the problem, including peer reviews of possible alternative methods by a subpanel of the FIFRA Scientific Advisory Panel, the Agency published a new regulatory policy last May. Our new policy allows applicants for registration to chose from three testing options for demonstrating the efficacy of their tuberculocidal products, (1) the standard AOAC method; (2) the AOAC method with substantial modifications; and (3) a new quantitative method.

The new policy applies to holders of existing registrations as well as applicants for new registrations, and it includes provision for verification of the validity of suspect efficacy claims and for demonstrating reuse capacity. Verification testing, when required, must be conducted by a second independent laboratory. Significant progress has been made toward the development of a reproducible test for the efficacy of disinfectant solutions.

QUALITY CONTROL

Once we have tests which satisfy those criteria, we must have quality assurance. The public must have meaningful assurance that each pesticide lot does indeed meet EPA requirements. Antimicrobials have been regulated, to some extent, since 1912, and the Agency has learned from that experience. EPA, and prior to 1970, USDA, have required and continue to require efficacy testing prior to registering antimicrobial pesticides. As with other types of pesticides, as scientific knowledge increases, data requirements become more sophisticated. Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), Congress clearly placed the burden of proof on the registrant to show that a registered pesticide is efficacious and does not pose unreasonable risks to people or the environment. To carry out the purposes of the Act, the Agency requires applicants for registration to submit efficacy data specific to each product that bears a claim to control organisms which may pose a threat to human health, either directly or through transmittal of disease.

In the past, the Agency conducted a token amount of efficacy testing at the Beltsville, Maryland laboratory. The antimicrobial testing conducted at Beltsville either duplicated selected studies submitted in support of product registration or, for enforcement purposes, assessed the efficacy of samples from batches of products in the marketplace. The pre-registration testing was extremely limited, primarily to confirm sterilization claims and selected tuberculocidal claims.

The Agency's post-registration testing for the 16 year period prior to 1982 included just under 6,000 products and showed a failure rate of about 15-16%. During that period, the majority of the products tested were selected for testing because of earlier failures. [These results are consistent with Florida statistics for products tested in 1982: Of those tested, about 10-15% of the samples failed. The reasons for failure were shown to be product related (rather than problems with the test) in many, if not most, cases.]

Testing of antimicrobial products at the Beltsville lab was phased out in 1982 for several reasons:

1. The efficacy testing at Beltsville was inadequate. Before a registration was granted, the registrant carried out extensive testing to gain approval, and then in the few cases where samples were tested, the federal government merely conducted a few screening tests.

2. The Agency recognized a serious need to update test methods as a first step toward improvement of the program. Without a reliable test method, the value of any monitoring or

enforcement program is greatly diminished if not lost. In freeing the Beltsville lab from routine testing, more time and effort could be directed toward the evaluation and improvement of test methods.

3. It became apparent that the Beltsville program was creating a false sense of security among users and the public in general. Even today, we still hear the echoes of the misunderstanding that the testing at Beltsville somehow assured the efficacy of disinfectants prior to 1982. The fact is that preregistration screening was carried out only infrequently, and during the last 10 years of the program, of the tens of thousands of batches of the roughly 20,000 antimicrobial products registered, the number of samples tested for enforcement purposes averaged about 125/year. I am sure you will agree that this was a less thorough testing program than would be needed to assure efficacy. The Agency also hoped that removing the false security blanket of federal testing would make users more vigilant and would encourage a more active role by the user community and state governments in surveillance of product efficacy.

The Agency's decision to discontinue the Beltsville program in 1982 should not be construed as an abandonment of EPA's strong commitment to public health protection. Rather, the issue is a question of how such protection can be achieved most effectively and in the most cost effective manner.

There are several possible approaches to quality assurance, none of them simple, each with its own advantages, and the quality control function will be a central element of our strategy. For example, the Agency is considering whether it can require the registrant to conduct efficacy testing on a lot by lot basis through regulation, or whether the Agency could require the registrant to employ a third party laboratory, approved by EPA, to conduct verification testing. The Agency already uses some outside groups, such as the SAP and others, to help review protocols, and there may be additional ways of making use of their expertise.

PREVENTION OF TOXIC EFFECTS

In addition to assurance that a product is effective against the target pest, FIFRA requires a finding that its use will not result in unreasonable adverse effects on people or the environment. The Agency therefore requires the submission of data to evaluate the toxicity of pesticides and their potential to adversely affect non-target organisms, including people.

As you know, EPA has been directed by Congress to reevaluate the data bases and reregister all pesticides registered before 1978. In the course of its reregistration activities, the Agency has been looking at the quality of the data bases for antimicrobial pesticides. As I mentioned earlier, antimicrobials give rise to particular concern about their efficacy, but the need for efficacy data should not overshadow the necessity of adequate exposure and toxicity data. In 1985 the Agency established a work group to review the Agency's policies regarding toxicology data requirements for antimicrobial products. The work group concluded that a tiered testing system should be implemented. The system would first require some minimum level of toxicity and exposure data for all products; then if a product meets certain criteria indicating potential to cause adverse effects, a second tier of studies would be required, and so on. We believe that such a system will give Agency scientists enough data to make sound judgments, and at the same time avoid unnecessary financial burdens for industry as well as Agency resources. We anticipate issuing letters by the end of this year requiring all registrants to submit appropriate data pursuant to FIFRA section 3(c)(2)(B).

ACCURATE LABELING AND ADVERTISING

Finally, to protect the public from relying on false claims of efficacy by disinfectant manufacturers, it is important to have strict controls on labeling and advertising. This aspect of antimicrobial regulation has raised serious concerns in the past year. The Agency's attention was focused on this problem by recent claims by manufacturers that their products were effective against the Hepatitis B and AIDS viruses. Under section 2(ee) of FIFRA, a pesticide may be used against a pest other than the one originally specified as long as the use is not specifically prohibited by the approved label. Therefore, the Agency's policy has, in the past, allowed the advocacy of uses against pests in addition to those approved by EPA, as long as the use site was approved and the use was not otherwise prohibited.

However, the Agency reconsidered that policy with respect to antimicrobials and concluded that, for antimicrobial products, efficacy claims that are not supported by efficacy data may foster a false sense of security among health professionals relying on use of that product. Since the presence of the target microorganism cannot readily be discerned by users, they cannot easily judge for themselves the effectiveness of the product. In order to protect public health, the Agency decided that a new policy was necessary for antimicrobial pesticides which are used against human pathogens. The new policy, which was published in the Federal Register last May, prohibits anyone with a financial interest in one of these products from making any claims for it which differ from those on the EPA-approved labeling. EPA's Office of Compliance Monitoring sent notices to each company reported to be making such claims, advising them of the new policy. Thus far the results have been good, but the Agency has made it clear that any future violations will meet with strict enforcement measures.

In conclusion, let me repeat--the Agency is working to improve the disinfectants program, and progress is being made. We anticipate having a new strategy ready around the first of the year. Meanwhile, the Agency has several ongoing activities which will continue: We have one new test method and will soon be ready to implement improvements to the Use Dilution Test; we have reevaluated our toxicity data requirements and are about to issue a new data call-in; we have notified registrants of tuberculocides of new efficacy data requirements; and we have cracked down on possibly misleading advertising. We are looking for and evaluating new approaches to improve the program, but we are taking steps now to make this a strong regulatory program with aggressive oversight.

I would be happy to answer any questions you may have.

Senator **Sarbanes**. Thank you. Dr. Rheinstein, I think we'll hear from you and then proceed with questioning.

STATEMENT OF PETER H. RHEINSTEIN, M.D., DIRECTOR, OFFICE OF DRUG STANDARDS, CENTER FOR DRUGS AND BIOLOGICS, FOOD AND DRUG ADMINISTRATION

Dr. **Rheinstein**. Mr. Chairman, my name is Peter Rheinstein. I am Director of the Office of Drug Standards within the Center for Drugs and Biologics at the Food and Drug Administration.

I am here today to discuss with you the problem of nosocomial infections and the regulation of topical antimicrobial products, especially those use in hospital settings.

HOSPITAL ACQUIRED INFECTIONS

Nosocomial, or hospital acquired, infections are a significant health problem in the United States today. The most recent surveillance date compiled by the Centers for Disease Control, or CDC, indicate that in 1984 the overall rate of nosocomial infections was 3.4 per 100 patients discharged, with essentially no change in infection rates or associated mortality rates compared to the 3-year surveillance period 1980 to 1982. A retrospective study of a representative sample of U.S. hospitals in 1975 and 1976 found infection rates of 5 to 6 percent and other authorities have cited estimates of 5 to 10 percent. Morbidity, mortality and associated costs of patient care are significant.

A number of factors contribute to patients acquiring infections in hospitals. For example, with respect to postoperative wound infections, pathogenic organisms from the patient, foreign bodies, or the hospital environment may cause infections. Predisposing factors include operative techniques, including basic cleanliness; location of the wound; type of surgery, for example, gunshot wounds versus "clean" surgery; the existence of devitalized tissue; the existence of remote sites of infection in the patient; and the patient's general physical condition and immune status, factors which may account for the higher rates of nosocomial infections found in some teaching hospitals with "sicker" patients. Shaving the patient in advance of surgery may also be implicated. Catheterization, especially if prolonged, and any other invasive medical practice which "breaks the system" increases risk. Inadequate sterilization may lead to complications. Gases used in anesthesia and the patient's history of smoking and alcohol use can impair the functioning of defense mechanisms in the lungs, increasing the risk of respiratory infections.

PHS ACTIVITIES

The Public Health Service has an active interest in nosocomial infections, and FDA and CDC in particular have been involved in a variety of activities, including: outbreak investigation; surveillance; identification of risk factors and modes of transmission; the development and evaluation of prevention strategy; training of hospital personnel; and development of diagnostic laboratory techniques.

A number of guidelines to assist hospitals in establishing sound infection control programs have been issued. I would be pleased to provide a description of these activities for the record.[1] In addition, hospital accrediting bodies such as the Joint Commission on the Accreditation of Hospitals set standards in this important area.

In summary, hospitalized patients may acquire infections from their own flora, other patients, or transmission by health care personnel, usually on the hands of health care workers who move from patient to patient. Inadequate personal hygiene—failure to wash hands—is a primary culprit, nearly a century and a half after its critical importance to patient health was first demonstrated. No soap or scrub works if it is not used, and all too frequently it is not.

The essential components of effective hospital programs include a balance between intensive surveillance and intensive control efforts. The availability of epidemiological expertise, infection control nurses and surveillance of postsurgical wound infection rates and reporting them to surgeons were identified as effective by the Study on the Efficacy of Nosocomical Infection Control, SENIC, a large-scale, 10-year study of this important problem. Programs with these components were found to be capable of preventing approximately one-third of those infections that would otherwise occur.

REGULATION OF PRODUCTS

Thus, many of the most effective means of infection control are primarily related to improving clinical conditions and hygienic practices in hospitals. However, FDA's regulatory mission also involves efforts aimed at ensuring that products subject to our jurisdiction are safe and effective. These include topical antimicrobial products for use on the body such as health-care personnel handwashes, patient preoperative skin preparations, and surgical hand scrubs.

In summary, the Federal Food, Drug, and Cosmetic Act requires that drugs such as topical antimicrobial products undergo premarket approval for safety and effectiveness if they are "new drugs," that is, not generally recognized by experts as safe and effective for their intended use. The FDC Act also requires that all drugs must be free from adulteration and labeled in a manner that is not false or misleading.

Premarket approval involves the submission of a new drug application that provides FDA with scientific data demonstrating that the particular drug is safe and effective. A number of widely used antiseptics have been approved in this manner.

Most antiseptic products, however, fall within the purview of FDA's over-the-counter, OTC, drug review and may be marketed without an approved application by complying with ingredient and labeling requirements established by FDA for OTC drugs that are generally recognized by experts as safe and effective.

Since 1978, we have been receiving safety and effectiveness data based on testing protocols and guidelines developed by the agency for topical antimicrobial ingredients identified as needing further study. Where data were lacking, the outstanding safety issues generally focused on whether there was any long-term toxicity to individuals who used these products as often as several times a day over many years. To answer this question, long-term toxicity studies in animals were needed. These studies take many years to conduct. For those ingredients with effectiveness questions associated with them, the questions tended to focus on the speed of action; that is, whether they killed microbes quickly enough. Their ability to kill microbes was generally already established.

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[1] See the end of Dr. Rheinstein's oral statement for a description of activities provided for the hearing record.

A considerable amount of data have been generated and submitted to FDA for review. We now know that the ingredients originally identified as not safe and effective for specific hospital uses are not, in fact, being used in products labeled for those specific purposes. Finally, the considerable data that have been generated have resolved many original questions about the safety and effectiveness of topical antimicrobial ingredients.

FDA scientists have completed a preliminary review of the new data, which will form the basis for a Federal Register document announcing our conclusions on the uses of these OTC products and appropriate labeling requirements. Although reports implicating the use of these products as a significant factor in hospital acquired infections are uncommon, we are committed to a thorough review of their safe and effective use.

This completes my statement. I will be happy to answer any questions you may have. Due to the shortness of time, we have not yet completed compiling detailed answers to all of the questions of your September 19 letter. I will be glad to provide more detailed information for the hearing record.

[The information referred to for the hearing record by Dr. Rheinstein follows:]

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Chemical Disinfection of Medical and Surgical Materials

M.S. FAVERO, PH.D.

The effective use of proper disinfectants and sterilization procedures constitutes a significant factor in preventing nosocomial infections. Physical agents such as moist or dry heat play the dominant role in sterilization procedures in hospitals, and chemical germicides are used primarily for disinfection and antisepsis. In recent years, there has been a virtual explosion in the numbers and types of chemical germicides available to health professionals in the United States. In 1973, the American Society for Microbiology Ad Hoc Committee on Microbiologic Standards of Disinfection in Hospitals surveyed 16 hospitals in various parts of the United States with a combined bed capacity of more than 9000 and found that the average number of different formulations per hospital was 14.5, with a range of 8 to 22. A total of 224 products were used in the 16 hospitals, and 120 of them were proprietary products.

In 1981, the Hospital Infections Program, Centers for Disease Control, Atlanta, Georgia, developed a set of guidelines for the prevention and control of nosocomial infections (CDC, 1981). These guidelines, which will be updated periodically, are provided to all hospitals in the United States. They should be consulted for current information and recommendations for environmental control and prevention of nosocomial infections.

The choice of specific disinfectants in association with protocols for cleaning is a decision that is made broadly and at various levels of hospital and other health care environments. It is evident that no single agent or procedure is adequate for all disinfection or sterilization purposes and that the realistic use of chemical germicides depends on a number of factors that should be considered in choosing among the available procedures. These include the degree of microbial killing required, the nature and composition of the item or device to be treated, and the cost and ease of use of the available agents. This chapter deals with each of these factors and discusses practical methods for evaluating the effectiveness of the various agents and procedures.

CATEGORIES OF MATERIALS

As used in this chapter, the term "medical and surgical materials" includes instruments, equipment, and medical devices, the use of which involves significant risk of transmitting infection to patients or hospital personnel. Consequently, these items should be either sterilized or disinfected to prevent cross-contamination and infection.

The nature of instrument and equipment disinfection can be understood more readily if medical devices, equipment, and surgical materials are divided into three general categories based on the risk of infection involved in their use. These categories were first suggested by Dr. E.H. Spaulding (1972; Spaulding et al., 1977). Although one risks oversimplification in dividing medical devices into such categories, I have elected to retain Dr. Spaulding's classification system because it is fairly straightforward and logical and has been used for years by epidemiologists and microbiologists when discussing or planning strategies for disinfection and sterilization.

Spaulding believed that strategies for sterilization and disinfection could be better understood and implemented if equipment and items for patient care were categorized by the degree of infection risk involved in their use. He described three categories of such items: critical, semicritical, and noncritical.

Critical items, the first category, are so called because the risk of acquiring infection is great if such an item is contaminated. These are instruments or objects that are introduced directly into the human body—either into the blood or into normally sterile areas of the body. Examples are scalpels, transfer forceps, cardiac catheters, implants, pertinent components of the heart-lung oxygenator, and the blood side of artificial kidneys. The requirement for these items prior to use is sterility, and consequently, one of several accepted sterilization procedures should be chosen.

Items in the second category are classified as semicritical in terms of the degree of risk of infection; examples are flexible fiberoptics, endotracheal and aspirator tubes, bronchoscopes, respiratory therapy equipment, cystoscopes, and urinary catheters. Although these items come in contact with intact mucous membranes, they do not ordinarily penetrate body surfaces. Sterilization of many of these items, although desirable and often more cost-effective if steam autoclaves can be used, is not absolutely essential. Semicritical items should be subjected, at a minimum, to a procedure that can be expected to destroy ordinary vegetative bacteria, most fungal spores, the tubercle bacilli, and small nonlipid viruses. In most cases, meticulous physical cleaning, followed by an appropriate high-level disinfection treatment, gives a reasonable degree of assurance that the items are free of pathogenic microorganisms.

A third category is noncritical items. These do not ordinarily contact the patient directly or, if they do, contact only unbroken skin. Such items include face masks, humidifiers, rebreathing bags, x-ray machines, and a variety of accessory medical and surgical items. Use of these items carries relatively little risk of transmitting infection. Consequently, depending on the particular piece of equipment or item, cleansing with a good detergent in hot water may be sufficient, but with some, the added assurance of chemical disinfection with a low-level disinfectant may be appropriate.

If all medical and surgical materials could be sterilized by steam autoclaving, there would be no need to establish these categories. In reality, however, many such medical devices and articles in everyday use cannot be sterilized by steam autoclaving or irradiation, and chemical germicides must be used. In this context, one must then consider the differences between chemical sterilization and chemical disinfection.

ANTIMICROBIAL EFFECTIVENESS OF CHEMICAL GERMICIDES: DEFINITION OF TERMS

Although the definitions of sterilization, disinfection, and antisepsis (Spaulding, 1972; see also Chapter 44) have been generally accepted, it is common to see all three terms misused, especially by health professionals in hospitals. The exact distinction among the three terms and the basic knowledge of how to achieve and monitor each state are important if long-known principles are to be effectively applied.

Sterilization

Sterilization is defined as the use of a physical or chemical procedure to destroy all microbial life, including highly resistant bacterial endospores. In the hospital, this pertains particularly to those microorganisms that may exist on inanimate objects. Moist heat by steam autoclave, ethylene oxide gas, and dry heat are the major sterilizing agents used in hospitals. As will be seen, however, there are a variety of chemical germicides that have been used for purposes of sterilization and that appear to be effective when used appropriately. These germicides, used in a different manner, actually may be part of a disinfection process. Unfortunately, some health professionals refer to "disinfection" as "sterilization," which leads to a degree of confusion that often becomes magnified with routine use. A good example of this is the use of 2% glutaraldehyde germicides for the disinfection of certain flexible fiberoptic endoscopes. Some practitioners refer to this as "sterilization" of endoscopes. A 2% glutaraldehyde solution is capable of sterilization, but only after extended contact time in the absence of extraneous organic material. Unfortunately, flexible fiberoptic endoscopes are not physically capable of withstanding immersion in fluid for 6 to 10 hours—in fact, most manufacturers recommend that immersion times not exceed 10 minutes. Thus, the procedure the endoscopes are subjected to is one of disinfection and not sterilization, in spite of the fact that colloquially it is referred to in the hospital as "sterilization."

Disinfection

Disinfection is generally a less lethal process than sterilization. It eliminates virtually all recognized pathogenic microorganisms, but not necessarily all microbial forms (e.g., bacterial endospores), on inanimate objects. As can be seen by this definition, disinfection does not ensure an "overkill," and disinfection processes lack the margin of safety achieved by sterilization procedures. The effectiveness of a disinfection procedure is controlled significantly by a number of factors, each of which may have a pronounced effect on the end results. Among these are the nature and number of contaminating microorganisms (especially the presence of bacterial endospores), the concentration of and length of exposure to the germicide, the amount of organic matter (soil, feces, blood) present, the type and condition of the medical and surgical materials to be disinfected, and the temperature.

Disinfection then is a procedure that reduces the level of microbial contamination, but there is a broad range of activity extending from sterility at one extreme to a minimal reduction in the number of microbial contaminants at the other. It is emphasized that the acceptance of such distinctions is consistent with the ability of a nonsporicidal disinfectant solution to *completely destroy* microbial contamination on medical and surgical materials. Indeed, this probably happens often when spores are absent. Nevertheless, it should not be called sterilization; one would expect that microbiologic assays would be negative only when the item was free of bacterial spores, because of the way it was either used or cleaned or both. This is an important achievement, and consequently there is a need for a term to distinguish between sterilization and the destruction of microbial contamination that is free of bacterial endospores. *Decontamination* is the most appropriate term to be used in this sense, and it implies that items and devices treated as such are rendered safe to handle.

By definition, chemical disinfection differs from sterilization by its lack of sporicidal power. This is an oversimplification of the actual situation, because a few chemical germicides in fact do kill spores, although they may require a high concentration and several hours to do so.

Nonsporicidal disinfectants may differ in their capacity to produce decontamination. Some germicides kill rapidly only the ordinary vegetative forms of bacteria such as staphylococci and streptococci, and some forms of fungi and lipid-containing viruses, whereas others are effective against such relatively resistant organisms as the tubercle bacillus, *Mycobacterium tuberculosis*, other fungi and nonlipid viruses. The latter group therefore represents a level of activity between that of sporicides and many commonly used germicides. Furthermore, absolute sterility is difficult to prove, and as a result, sterility is commonly defined in terms of the probability that a contaminating organism will survive treatment. For example, sterilizing processes are challenged usually with a high number (10^6 to 10^7) of dried bacterial endospores, and sterilization is defined as the state in which the probability of any one spore surviving is 10^{-6} or lower. As pointed out in other chapters in this book, this rationale has been used to establish cycles for steam autoclaves and ethylene oxide gas sterilizers, and it produces a great degree of overkill as well as a quantitative assurance of true sterilization. It is virtually impossible to evaluate liquid chemical disinfection processes by using these criteria, and disinfection procedures cannot be assumed to have the same reliability as sterilization procedures.

Antisepsis

An *antiseptic* is defined as a germicide that is used on skin or living tissue for the purpose of inhibiting or destroying microorganisms. Antiseptics are not discussed in this chapter because they are treated elsewhere in this book, but it should be realized that the distinction between an antiseptic and a disinfectant often is not made. As defined, a disinfectant is a germicide that is used solely to destroy microorganisms on inanimate objects; an antiseptic germicide, however, is one that is used on or in living tissue. Although some specific germicides may be used for both purposes (e.g., alcohols), the adequacy for one purpose does not ensure adequacy for the other. Consequently, it is not good practice to use an antiseptic for the purposes of disinfection and vice versa, because manufacturers specifically formulate germicides for their intended use.

LEVELS OF DISINFECTION

As mentioned previously, Spaulding categorized medical and surgical materials into critical, semicritical, and noncritical items. He also proposed three levels of germicidal action to be recognized for properly carrying out strategies for disinfection in hospitals. The terms "high," "intermediate," and "low" will be used to designate these levels of germicidal action (Table 25–1).

High-Level Disinfection

A number of critical items are damaged by high temperatures, cannot be heat sterilized, and must be disinfected with chemical germicides. As can be seen from Table 25–1, an essential property of a high-level disinfectant is effectiveness against bacterial endospores; usually, if the contact time is long enough, this type of germicide can be used as a sterilant. High-level disinfectants are used often to treat medical and surgical materials, and in the absence of bacterial spores, they are rapidly effective. The absence of spores usually cannot be ensured, although it has been shown that the number of spores on items subjected to such treatments is generally low (Spaulding, 1939). The sporicidal activity of the high-level disinfectant depends on both the specific chemical agent and the manner in which it is used. Table 25–2 shows several disinfectants categorized as having high-level activity. These include aqueous 2% glutaraldehyde, 8% formaldehyde solution in 70% alcohol, 6 to 10% stabilized hydrogen peroxide, and ethylene oxide gas.

In addition, a number of germicides are available commercially that have been approved by the U.S. Environmental Protection Agency (EPA) as sterilants and sporicides. As will be pointed out later, the Association of Official Analytical Chemists (AOAC) sporicidal test is highly stringent, so that chemical germicides designated as sporicides or sterilants by the AOAC are most likely effective. Some of these products combine various chemicals, such as glutaraldehyde with formaldehyde and glutaraldehyde with phenol and phenate. Peracetic acid in liquid and vapor has been described in the past as a high-level disinfectant, but its application presents major difficulties (Portner and Hoffman, 1968; Hoffman and Warshowsky, 1958), especially with medical and surgical items.

Germicides classified as sporicides have been shown to kill large numbers of resistant bacterial endospores under stringent test conditions, but may require as long as 24 hours of contact time to do so (Ortenzio, 1966). Although this type of germicide may qualify technically as a cold sterilant because of the time involved, it may receive little use. In addition, most medical devices in actual practice are not contaminated with extraordinarily high levels of bacterial endospores, so that if a small number of spores comprised the initial population, sterilization may occur much more quickly than 24 hours (Spaulding, 1963, 1972). In other words, given the circumstances of relatively

TABLE 25–1. LEVELS OF GERMICIDAL ACTION

	Bacteria			*Fungi**	*Viruses*	
	Vegetative	*Tubercle bacillus*	*Spores*		*Lipid and medium-size*	*Nonlipid and small*
High	+†	+	+	+	+	+
Intermediate	+	+	−	+	+	+
Low	+	−	−	±	+	

*Includes usual asexual "spores," but not necessarily chlamydospores and sexual spores.

†Plus signs indicate that a microbicidal effect can be expected when the normal use-concentrations of disinfectants are properly employed.

TABLE 25–2. ACTIVITY LEVELS OF SELECTED GERMICIDES

Class	*Use-Concentration of Active Ingredient*	*Activity Level*
GAS		
Ethylene oxide	450-500 mg/L[*]	High
LIQUID		
Glutaraldehyde, aqueous[†]	2%	High
Formaldehyde + alcohol	8% + 70%	High
Stabilized hydrogen peroxide	6 to 10%	High
Formaldehyde, aqueous	3 to 8%	High to intermediate
Iodophors[‡]	30 to 50 mg/L free iodine/ 70 to 150 mg/L available iodine[‡]	Intermediate
Iodine + alcohol	0.5% + 70%	Intermediate
Chlorine compounds	0.1 to 0.5% free chlorine	Intermediate
Phenolic compounds, aqueous	0.5 to 3%	Intermediate to low
Quaternary ammonium compounds	0.1 to 0.2% aqueous	Low
Mercurial compounds	0.1 to 0.2%	Low

[*] In autoclave-type equiment at 55° to 60° C.

[†] There are several proprietary formulations on the U.S. market, i.e., 4% glutaraldehyde and 3% formaldehyde; glutaraldehyde 2% and 7% buffered phenol; and glutaraldehyde 2%, low pH and normal and raised temperatures.

[‡] See text for a discussion on semantic problems associated with iodophors, available iodine, and free iodine.

few bacterial spores present, sterilization can be achieved by a weaker germicide. Since medical devices and items are not routinely monitored microbiologically, however, one cannot consistently ensure the absence of bacterial spores, so that with certain critical types of medical devices, it may be good practice to rely on those germicides that have been documented in the scientific literature to produce a sporicidal effect in a given amount of time and/or approved by the EPA as sporicides or sterilants.

In any event, these germicides can be relied upon to produce sterility if the exposure elements in terms of contact time, temperature, pH, and other variables are met. A sterilization process accomplished by a chemical germicide gives less assurance than one accomplished by a physical process such as steam autoclaving or dry heat. The latter procedures are much less prone to be affected by human error than those associated with chemical germicides.

One question that is raised consistently is whether high-level germicides should be designated as sterilizing agents. Ethylene oxide, for example, has been widely accepted and officially recognized as a sterilizing agent. In reality, however, its sterilizing capacity varies significantly with the procedures used because ethylene oxide is a chemical disinfectant and is subject to the same factors that influence the antimicrobial efficacy of other germicides. Ethylene oxide sterilization processes performed by large pharmaceutical houses in the United States and elsewhere employ prehumidification, heating, and evacuation of the chamber, and high concentrations of the gas in operating cycles as long as 20 hours. If this process is carried out properly, one can verify sterility as the end result.

Ethylene oxide sterilizers that are commercially available to health care practitioners and that are used in hospitals, medical offices, and other settings display such a wide variation in design and use that ethylene oxide sterilization sometimes cannot be verified. Usually, commercially available large-chamber ethylene oxide sterilizers can consistently sterilize medical items. When these are challenged with high numbers of bacterial endospores (10^{6} to 10^{8}), exposure times of 8 to 12 hours appear to be satisfactory for achieving sterility. This is primarily owing to the sophisticated physical controls regulating temperature, relative humidity, and such prerequisites as prehumidification and evacuation of chambers. Smaller types of sterilizers using ethylene oxide gas are often less reliable in achieving sterility because such critical factors as prehumidification, heating, evacuation, and delivery of ethylene oxide gas under pressure are either absent or inconsistent. With these types of "sterilizers," much more time may be required to achieve sterility, especially when the challenge consists of large numbers of bacterial spores. If the challenge consists of vegetative bacteria or naturally occurring microbial contamination on in-use medical devices and if the presterilization load of bacterial spores is low, sterility may be achieved, but there is less assurance regarding the effectiveness of the entire process.

The question of how many high-level germicides should be classified as sterilizing agents tends to be academic, because all of them take much longer than a steam autoclave. Although the AOAC sporicidal test is stringent and is a major criterion used by the EPA to designate a germicide as a sterilant, the actual procedures associated with the use of chemical germicides demand much more in the way of microbiologic verification because potency of the chemicals is affected by such factors as organic load, temperature, and contact time. The manufacturer's time and effort spent verifying the effectiveness of the sterilization process, as discussed in other parts of this book, are extensive and technically sophisticated. The same approach cannot be used in a modern hospital. About the best that can be done is, for example, the use of biologic indicators with ethylene oxide sterilizers.

There is no way to verify microbiologically the sterility of medical devices and items that are sterilized without sampling the item itself. The usual procedure is to verify that the germicide can inactivate 10^6 to 10^7 spores of *Bacillus subtilis* or *Clostridium sporogenes*. This can be determined in a laboratory, but variation caused by human error cannot be measured, so that the existence of an established set of procedures associated with the sterilization procedure and the germicide used takes on critical importance. A good example of this is the use of 2% glutaraldehyde germicides, which are capable of sterilization, but only after extended contact time and in the absence of extraneous organic material. Unfortunately, some materials are not physically able to withstand immersion in these fluids for 6 to 10 hours. Even if prolonged contact were possible, the treated materials would have to be rinsed thoroughly with sterile water, dried in a special cabinet with sterile air, and stored in a sterile container to ensure that the materials remain sterile. One can observe staff members in hospitals and other settings, however, soaking items in 2% glutaraldehyde germicides for 10 to 30 minutes, rinsing them in nonsterile water, and referring to the items as "sterile." This particular situation indicates a misunderstanding of the terms "sterile" and "disinfected," as well as overconfidence in a particular germicide and overestimation of the safety of the processed item.

Intermediate-Level Disinfection

Intermediate-level disinfectants do not necessarily kill large numbers of bacterial endospores in a relatively short time, i.e., 6 to 12 hours, but they do inactivate the tubercle bacillus, which is significantly more resistant to aqueous germicides than are ordinary vegetative bacteria. These disinfectants are also effective against fungi (asexual spores but not necessarily dried chlamydospores or sexual spores) as well as lipid and nonlipid medium-size and small viruses. Examples of intermediate-level disinfectants (Table 25–2) include 0.5% iodine, 70 to 90% ethanol and isopropanol, chlorine compounds (free chlorine, i.e., hypochlorous acid as derived from sodium hypochlorite, calcium hypochlorite or gaseous chlorine) at 500 mg/l. and some phenolic and iodophor-based disinfectants, depending on formulation.

Although intermediate-level disinfectants are considered effective against viruses, there appear to be some exceptions. Klein and Deforest (1963) have shown that the resistance of viruses to chemical disinfectants varies significantly. They reported that small nonlipid viruses were significantly more resistant to chemical germicides than medium-size viruses with lipid in their protein coats. Some of the most widely used liquid germicides failed to destroy picornaviruses, which include the enterovirus group and the rhinoviruses of the common cold. The point here is that simply because a germicide has good tuberculocidal activity, it cannot be assumed categorically that these germicides are effective against all viruses. Moreover, there are a number of viruses for which tissue culture systems are not yet available and for which documented laboratory testing with various germicides has not yet been accomplished. For example, the human hepatitis viruses (B, and non A/non B) have been difficult to study because they have not yet been cultured in the laboratory. There is no evidence, however, that any of these viruses are unusually resistant to physical or chemical agents (Miner, 1978). It has been proposed that the resistance level of the hepatitis B virus, for example, is between that of the tubercle bacillus and the bacterial spores, but nearer that of the former (Bond et al., 1977). Since there is a doubt, the most conservative approach would be to use high-level disinfectants for decontamination and disinfection when hepatitis B virus contamination is known or suspected.

Some chemical germicides with good tuberculocidal activity can destroy small nonlipid viruses. As shown by Klein and Deforest (1963), both 70% ethanol and isopropanol are rapidly tuberculocidal (Spaulding, 1964; Heister et al., 1968), whereas only the former was found by Klein and Deforest to destroy the small nonlipid viruses they studied. On the other hand, Wright (1970*a*) reported that ethanol failed to kill a test virus that, on the basis of Klein and Deforest's study, would be expected to be quite susceptible. At best, an intermediate-level tuberculocide may not necessarily be an intermediate-level virucide.

The germicidal resistance of fungi in general is probably similar to that of gram-positive vegetative bacteria (Prindle and Wright, 1968; Lawrence, 1968). Bacteriostasis may not have been eliminated in many of these reports, however, and there is now reason to believe that some forms of pathogenic fungi may be considerably more resistant than most vegetative bacteria (see Chapter 11). Since it is likely that germicidal chemicals that kill the more resistant fungi may not also be tuberculocidal and virucidal, intermediate-level microbicidal capabilities should be examined with separate classes of microorganisms and referred to specifically.

Low-Level Disinfection

Low-level disinfectants are those that cannot be relied upon to destroy, within a practical period of time, bacterial endospores, the tubercle bacilli, or small nonlipid viruses. These disinfectants may be useful in actual practice because they can kill rapidly vegetative forms of bacteria and fungi as well as medium-size lipid-containing viruses. Examples of low-level disinfectants are quaternary ammonium compounds and mercurials. In addition, the germicidal activity is flexible, depending on the concentration of the active ingredient. Disinfection levels of iodophors and phenolic compounds may be classified as intermediate or low depending on concentrations of the germicide. All germicidal chemicals do not have this capacity. For example, even a 5 to 10% concentration of a quaternary ammonium compound may fail to meet the tuberculocidal or virucidal criterion of intermediate-level disinfection (Klein and Deforest, 1963). A subjective appraisal of commonly used disinfectants is presented in Table 25–3.

SELECTION OF DISINFECTION LEVEL

Patient care equipment and items have been categorized as critical, semicritical, and noncritical, and the level of disinfection that should be used depends in part on the particular category and nature of the item and the manner in which it is to be used.

Critical Items

It would be useless to attempt to name all of the critical items and the large number of medical and surgical materials in use in today's modern hospitals. The concept of a critical item is clear; the user must make his or her own list. All but a few articles in this category are either commercially presterilized or autoclaved by the user. A few important critical items, however, are reused repeatedly and not autoclaved for one reason or another. Examples are the transfer forceps and its jar, an increasing number of plastic parts on medical devices, and hemodialyzers, as well as certain flexible fiberoptic devices. To sterilize these items, one must rely on proper use of certain high-level germicides. Thorough cleansing must always precede chemical disinfection of such items because the mechanical action alone can remove a large proportion of contaminating microorganisms and a good deal of organic material that may tend to inactivate the germicide. The number of bacterial spores is usually small, and they would not be expected to occur in relatively high numbers except when grossly contaminated objects have not been well cleansed; this fact should not be interpreted as a rationale to substitute chemical sterilization for autoclaving. To do so would lower safety standards; also, using high-level germicides is inconvenient because several hours must be allowed to ensure sterilization, and the exposed materials

TABLE 25–3. RELATIVE EFFICACY OF COMMONLY USED DISINFECTANTS*

	Disinfectant	Comment
GAS		
Ethylene oxide	3–4†	Sporicidal, toxic, good penetration. Requires relative humidity of 30% or more. Microbicidal activity varies with apparatus used. Absorbed by porous material. Dry spores highly resistant. Moisture must be present; presoaking most desirable.
LIQUID		
Glutaraldehyde, aqueous	3	Sporicidal, toxic. Active solution unstable.
Stabilized hydrogen peroxide	3	Sporicidal. Use-solution stable up to 6 weeks. Toxic orally and to eyes, mildly toxic to skin. Little inactivation by organic matter.
Formaldehyde + alcohol	3	Sporicidal, toxic, volatile; noxious fumes.
Formaldehyde, aqueous	1–2	Sporicidal, toxic; noxious fumes.
Phenolic compounds	2–3	Stable, corrosive, irritates skin. Little inactivation by organic matter.
Chlorine compounds	1–2	Fast action; inactivation by organic matter. Corrosive; irritates skin.
Alcohol	1	Rapidly microbicidal except for bacterial spores and some viruses. Volatile, flammable. Dries and irritates skin.
Iodine + alcohol	0	Corrosive, rapidly microbicidal, flammable. Causes staining, irritates skin.
Iodophors	1–2	Somewhat unstable, relatively bland, corrosive. Staining temporary.
Quaternary ammonium compounds	1	Bland; inactivated by soap and anionics; absorbed by fabrics. Old or dilute solution can support growth of gram-negative bacteria.
Mercurial compounds	0	Bland, much inactivated by organic matter; weakly bactericidal.

*The values given in this table are my subjective appraisals. More detailed information must be obtained from descriptive brochures, journal articles, and books. Selection of the most appropriate germicide for a particular situation should be made by the responsible personnel in each hospital based upon: (i) whether it is to be used as a disinfectant or an antiseptic; (ii) estimation of the level of antimicrobial action needed; and (iii) the hospital's scope of services, physical facilities, and personnel. Instruments, apparatus, and other objects should be cleansed to remove gross organic soil prior to the use of chemical disinfectants that coagulate protein so as to get good penetration of crevices and porous material. Instruments, as well as rubber and plastic tubing, must be rinsed or flushed with water before coming into contact with skin, and especially mucous membrane, to avoid irritation. For the same reason, aeration is necessary after exposure to ethylene oxide.

†Maximal practical usefulness in the hospital environment is indicated by 4, little or no usefulness by 0.

must be rinsed or aired aseptically and kept sterile before use.

One may debate the importance of an occasional bacterial endospore that may remain viable after a critical item has been disinfected. There have been no epidemiologic studies that can answer this question, but two points deserve mention. First, critical items should receive high-level, instead of intermediate-level, disinfection if this is feasible. Second, for disinfection of semicritical items, the disinfection level should be intermediate, if feasible, rather than low. The second point pertains to the comment that most bacterial spores are nonpathogenic and thus may be ignored without incurring significant risk of infection. The distinction between pathogenic and nonpathogenic species is vague and relative rather than absolute, and in today's hospital environment, the host's level of resistance is the decisive factor in determining whether or not infection will develop. Classic nonpathogens such as *Bacillus subtilis* can produce serious and even fatal infections in immunosuppressed and immunocompromised hosts (Farrer, 1963; Conrad et al., 1971; Tuazon et al., 1979).

Certain critical items deserve special attention. Sterility is essential for hypodermic needles because they enter deep tissues. Use of liquid germicides cannot guarantee sterility because of the narrow lumen. Fortunately, today the widespread use of presterilized disposable needles has almost eliminated the risky practice of reusing chemically sterilized needles. With the advent of disposable sterile items, there is an increasing practice, based on economic factors, of reusing these items. A good example is the artificial kidney. Hemodialyzers are manufactured and delivered to the user in a sterile state. Assurance that the item is sterile depends on the manufacturer's quality assurance and sterilization cycle verification programs. Fifteen to 18% of the chronic dialysis centers in the United States, as well as some in Europe, reuse these dialyzers (Deane et al., 1978). In spite of the fact that dialyzers can be appropriately cleaned and disinfected, however, they are not subjected to the same stringent sterilization cycles or controls performed by the manufacturer. In this instance, the liability shifts from the manufacturer to the user. So far, this practice appears to be safe if proper cleaning and disinfection procedures are used, but there have been occasions when human error has caused significant side reactions and infections associated with the reuse of dialyzers. In general, reuse of disposable items that are initially sterile is discouraged.

Noncritical Items

Noncritical items consist of a variety of objects and items that offer little risk of transmitting infectious agents. These include face masks, carafes, electrocardiogram electrodes, walls, floors, furniture, and other environmental surfaces that ordinarily do not come into contact with human mucous membranes. Many individuals rely upon hot water or cleansing with detergent in water for these items, but chemical disinfection is also widely practiced, with low-level disinfectants used either alone or in addition to the cleansing.

FACTORS INFLUENCING GERMICIDAL PROCEDURES

Microorganisms vary widely in their responses to physical and chemical stresses. Those most resistant to such stresses are bacterial endospores; few, if any, other microorganisms approach the broad resistance of endospores. A number of factors, some of which are associated with the microorganisms themselves and others with the surrounding physical and chemical environment, influence the antimicrobial efficacy of chemical germicides. Some factors are more important than others, but all of them should be considered when planning strategy for the chemical disinfection of medical and surgical materials.

Nature of the Material

The easiest surface to disinfect chemically is one that is smooth, nonporous, and cleanable, such as a scalpel blade. Crevices, joints, and pores constitute barriers to the penetration of liquid germicides and require prolonged contact times to accomplish disinfection; in fact, it is possible for a disinfection procedure to fail under these circumstances. This is also true of ethylene oxide gas, which has a high degree of penetrability. If microorganisms are entrapped in impervious spaces or within organic materials, the ethylene oxide sterilization procedure may fail, especially when the level of contaminating microorganisms is high and composed of bacterial spores. In the last 10 to 15 years, a number of devices have been made of heat-labile materials that require chemical germicides for sterilization or high-level disinfection. If sterilization is the objective of a treatment, contact times of 6 to 10 hours are required, and this is often detrimental to the material in the devices. For example, flexible fiberoptic endoscopes cannot be subjected to long contact times in liquid germicides without risking the eventual degradation of lenses and other components. It is for this reason that, if sterilization is to be accomplished, ethylene oxide sterilization is the only feasible treatment. Since these instruments are expensive and frequently used, some practitioners have elected to practice high-level disinfection rather than sterilization of these instruments.

The size of a medical device also limits the types of germicides that can be used and governs whether sterilization or high-level disinfection will be the intended treatment. If an instrument is too large to be conveniently immersed in solutions or placed in any ethylene oxide chamber, disinfection may be accomplished by wiping with a liquid. This would include primarily semicritical or noncritical devices.

Thus, the nature and use of a medical device or item may dictate the type and use of a chemical germicide. Practitioners should be aware of this, and when purchasing medical devices, at least one criterion should be the ease with which the device can be cleaned and sterilized or disinfected.

Number of Microorganisms Present

Under a given set of circumstances, the higher the level of microbial contamination, the longer must be the exposure to the chemical germicide before the entire microbial population is killed. This factor does not stand alone, because the amount of time necessary to inactivate 100 bacterial spores would be significantly longer than the time required to inactivate 100 cells of *Staphylococcus aureus* or most other ordinary vegetative bacteria. When considering a natural microbial population composed of various types of microorganisms that have different degrees of resistance to physical or chemical stress, the survivor curve with all factors controlled would be parabolic and not straight (as it might be if a pure culture of a particular microorganism were used). Furthermore, the most resistant microbial subpopulation, even though it may be present in a fairly lower concentration than the entire microbial population, tends to control sterilization or disinfection time (Bond et al., 1971). A practical illustration of this factor is shown in Table 25–4.

Innate Resistance of Microorganisms

As mentioned previously, microorganisms vary widely in their resistance to chemical germicides, and thus, the types that are present on medical items or surgical materials may have a significant effect on the time as well as the concentration of germicides needed for sterilization or disinfection. The most resistant types of microorganisms are bacterial spores, some of which are significantly more resistant to both chemical and physical stresses (Bond et al., 1970, 1977). In a broad descending order of relative resistance, considerably below that of bacterial endospores are the tubercle bacilli, fungal spores, small or nonlipid viruses, vegetative fungi, medium-size or lipid viruses, and vegetative bacterial cells. Obviously, the biggest difference in resistance is between bacterial spores and vegetative cells. Smaller but important differences exist between the tubercle bacillus and nonacid-fast bacteria and among viruses and fungi. The human hepatitis viruses (B and non A/non B) are difficult to place in this order; it has been estimated (Bond et al., 1977) that their resistance levels are intermediate between bacterial spores and the tubercle bacilli, but more probably toward the latter.

The differences in chemical resistance exhibited by various vegetative bacteria are relatively minor, except for the tubercle bacilli and other nontubercular but acid-fast mycobacteria (Carson et al., 1978), which, presumably because of their hydrophobic cell surfaces, are comparatively resistant to a variety of disinfectants, especially those in the low-level category. Among the ordinary vegetative bacteria, staphylococci and enterococci are somewhat more resistant than most other gram-positive bacteria. It is interesting to note that antibiotic-resistant "hospital" strains of staphylococci do not appear to be more resistant to chemical germicides than ordinary isolates. A number of gram-negative bacteria, such as *Pseudomonas*, *Klebsiella*, *Enterobacter*, and *Serratia*, also may show somewhat greater resistance to some disinfectants than other gram-negative bacteria. This may be significant, because many of these gram-negative bacteria are known to often be responsible for outbreaks of hospital infections, especially in compromised hosts.

Gram-negative water bacteria that have the ability to grow well and achieve levels of 10^5 to 10^7/ml in distilled, deionized, or reverse-osmosis water have been shown to be significantly more resistant to a variety of disinfectants in their "naturally occurring" state (i.e., isolated and grown in pure culture in water without subculturing on laboratory media) as

TABLE 25–4. EFFECT OF NUMBERS ON SPORICIDAL TIME* (Spaulding, 1971)

Spore Count (per blade)	*Test Procedure*	*Positive*	*Negative*
100,000	Dried blood blade	2 hrs	3 hrs
1,000	Dried blood blade	1 hr	2 hrs
10	Dried blood blade	–	30 min

**Bacillus subtilis* spores. Germicides: 8% HCHO-67% isopropanol + 0.5% hexachlorophene

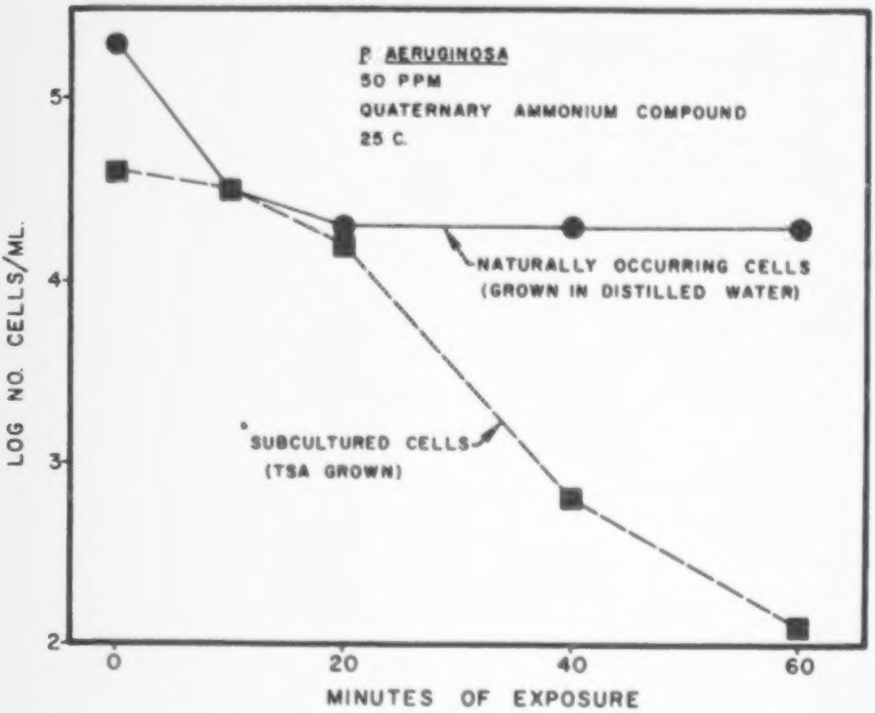

Fig. 25–1. Comparative survival of naturally occurring and subcultured cells of *Pseudomonas aeruginosa* exposed to a quaternary ammonium compound.

compared to bacterial cells subcultured in the normal fashion (Favero et al., 1975; Carson et al., 1972). Figure 25–1 illustrates this phenomenon, which has been shown to occur with nontubercular mycobacteria (Carson et al., 1978). These differences in resistance, although minor, become important when low-level disinfectants are used, particularly at marginal or dilute concentrations, or when disinfectants having greater germicidal properties are used inappropriately (e.g., ingredients used to prepare them are not fresh or significant organic loads are allowed to develop). The resistance of naturally occurring microorganisms also extends to bacterial spores, and it has been shown by Bond et al. (1970) that naturally occurring bacterial spores in soil are significantly more resistant to dry heat than those that are subcultured.

As will be discussed later, it is for these reasons especially that it is not sufficient to design a disinfection procedure solely on data acquired in laboratory tests such as the AOAC use-dilution procedure (AOAC, 1970). It is important also to base such procedures on data collected from actual in-use testing.

Amount of Organic Soil Present

Blood, mucus, or feces, when present on items that one intends to disinfect, may contribute to the failure of a given disinfection or sterilization procedure in two ways. The organic soil may occlude microorganisms and prevent penetration of chemical germicides, or the soil may directly and rapidly inactivate certain germicidal chemicals such as chlorine- and iodine-based disinfectants and quaternary ammonium compounds. This effect is correspondingly greater with weak concentrations and with low-level germicides than with strong concentrations and high-level germicides. In addition, this factor underscores the necessity and importance of thoroughly cleaning a medical device prior to chemical disinfection. Failure to do this prior to a procedure may cause failure of disinfection or sterilization.

In fact, physical cleaning is quite often the most important step in a disinfection process that, by definition, does not include the "overkill" factor of a sterilization process. Indeed, a report by Webb and Vall-Spinosa (1975) implicated a flexible fiberoptic endoscope in an outbreak of septicemia caused by *Serratia*. This instrument had been "sterilized" with ethylene oxide gas but had not been properly cleaned before the procedure. Consequently, even a rigorous cycle capable of killing exposed bacterial spores may not kill even relatively delicate vegetative bacterial cells if these cells are protected by extraneous organic material. This factor also is intimately associated with the number of microorganisms present, so that effective cleaning procedures that remove organic soil simultaneously tend to lower significantly the general level of microbial contamination associated with the soil.

Type and Concentration of Germicide Used

Generally speaking, with all other variables constant, the higher the concentration of a chemical agent, the greater its effectiveness and the shorter the length of time required to disinfect or sterilize an item. Generally unappreciated, however, are the wide differences in potency that exist among chemical germicides used for the same purpose. For example, Spaulding (1971) compared the tuberculocidal activity of several proprietary phenolic and iodophor-based compounds to that of isopropanol and determined that there were significant differences in the times required for disinfection (Table 25–5).

TABLE 25–5. TUBERCULOCIDAL ACTIVITY OF ALCOHOL PHENOLICS AND AN IODOPHOR

Compound	*Disinfection Times*
Phenolic I, 3%	2 to 3 hrs
Phenolic II, 3%	45 to 60 min
Iodophor, 450 ppm	2 to 3 hrs
Isopropanol, 70% vol	5 min

Simultaneous mucin-loop test. Number of *Mycobacterium tuberculosis* per loop was about 10^6.

Usually the disinfection time can be shortened significantly by increasing the use-concentration. Some chemical germicides are used appropriately only at strong concentrations. This is true for many of the high-level chemical germicides, such as formaldehyde, glutaraldehyde, and ethylene oxide, that are sporicides. It is also true of ethanol and isopropanol, because a dilution with water beyond 60 to 50% would reduce microbicidal activity. Some intermediate-level disinfectants may become useful sporicides when the concentration is increased significantly. This is probably true for hydrogen peroxide, but it is not true for all intermediate-level disinfectants.

In addition, iodine solutions and complexed iodine represent an instance in which confusion has existed with regard to chemistry and strategies of use.

As discussed in Chapter 8 and in the following, iodophor disinfectants are significantly affected by the amount of potassium iodide and water used in their formulation. Consequently, the label instructions describing a particular use-dilution for an iodophor are much more critical than for other chemical germicides because in the case of iodophors, use-dilution is geared to yield the maximum amount of free iodine possible. Under- or overdiluting the disinfectant may significantly reduce its germicidal potency. In other words, if an iodophor disinfectant is meant to be diluted 1:213, an undiluted or 1:10 aqueous dilution may have less microbicidal activity than the use-dilution. Furthermore, it is not clear what iodine species should be used to gauge germicidal potency. Most iodophor disinfectants and antiseptics are formulated to contain a certain amount of complexed iodine yielding a certain percentage of available iodine with usually an unspecified amount of free iodine contained in the use-dilution solution. Available iodine, which is simply the amount of iodine in solution that titrates with sodium thiosulfate, is not microbicidal. Certainly, the amount of available iodine present is important because it can be converted to free iodine depending on a number of other factors, including the amount of water present. Consequently, the manufacturer's instructions for proprietary iodophor preparations should be followed carefully so that the proper use-dilutions of the germicides are made. In any event, available iodine alone cannot be used to indicate germicidal potency. In fact, Berkelman and co-workers (1981) have shown that a 10% povidone-iodine solution containing 1% of available iodine but 1 ppm of free iodine was intrinsically contaminated with a vegetative bacterium, *Pseudomonas cepacia*.

Duration and Temperature of Exposures

As one might expect, with all other variables constant, the longer the germicidal process is continued, the greater is its effectiveness. An exception would be with some low-level disinfectants for which there might be a minimum threshold of the chemical that may have absolutely no effect on the microbial population. For example, some quaternary ammonium disinfectants used either in insufficient concentrations or in solutions that have deteriorated with age or because of the presence of organic soil not only might fail to affect some microbial populations (especially gram-negative bacteria), but may actually support their growth.

An increase in the temperature of a germicidal solution during the exposure time can significantly increase the efficacy of chemical germicides. One must take care, however, that the temperature does not exceed the point at which the germicide itself degrades, reducing its potency or creating a health hazard by producing toxic fumes. This is especially true with germicidal disinfectants whose active components are halogens or formaldehyde.

COMMONLY USED INSTRUMENT-EQUIPMENT GERMICIDES

As discussed previously, chemical germicides that are classified as disinfectants are, by definition, liquids or gases that are used specifically to inactivate microorganisms on inanimate objects. They are classified usually by activity as high-, intermediate-, or low-level disinfectants. The type of disinfectant that is chosen to accomplish a particular level of disinfection is related primarily to the item being disinfected, and whether that item is critical, semicritical, or noncritical in terms of risk of transmitting infection.

Variables discussed previously, such as the nature of the material, the level of microbial contamination, and the temperature and concentration of disinfectant, are important in the overall disinfection process. Further, in the hospital environment, one of the most critical factors affecting the successful outcome of the disinfection process is the efficiency of the procedure that is used to physically clean an instrument prior to disinfection. Without proper cleaning, most disinfection processes are subject to failure. The chemical germicides discussed in the following are those that are commonly used in hospitals in the United States.

Mercurials

Relatively high concentrations of mercurials are required to achieve significant bactericidal activity. They are fairly low-level disinfectants and have virtually no role in modern disinfection strategies.

Phenolic Compounds

Phenol or carbolic acid is one of the oldest antibacterial agents used in the hospital environment. The parent chemical has been replaced by hundreds of derivative compounds, referred to as phenol derivatives or phenolics. They are considered intermediate- to low-level disinfectants and are used primarily for disinfection purposes in general housekeeping and for noncritical items. The mechanism of action of phenol in high concentrations on the microbial cell appears to be that of a gross protoplasmic poison penetrating and destroying the cell wall and precipitating cellular protein (Prindle, 1968).

In lower concentrations, the eventual death of the bacterial cell appears to be due to inactivation of essential enzyme systems. Phenolics are considered fair to good bactericides in that they are stable and remain active after mild heating and prolonged drying. Subsequent application of moisture to a dry surface previously treated with a phenolic can redissolve the residual chemical so that it again becomes bactericidal. Concentrations of phenolics in the order of 1 to 2% remain active when in contact with organic soil. For this reason, phenolics are among the disinfectants of choice when dealing with gross fecal contamination.

Their usefulness for the disinfection of semicritical items is limited, however, because phenolics as a class are absorbed through porous materials, and the residue may irritate tissue.

Even when disinfected articles can be rinsed thoroughly before use, there is a possibility of residual disinfectant causing tissue irritation. Kahn (1970) reported that equipment and devices so treated caused depigmentation of skin and injury to mucous membranes. Brayman and Songer (1971) pointed out another aspect of phenol toxicity when they found hazardous concentrations in laboratory air near solutions that had been heated up to 45° C (Wysowski et al., 1978). For these reasons and because they are not good sporicides, phenolics are not useful for disinfection of critical and semicritical items. Phenolics have been shown to be effective but rather slow tuberculocides (Table 25-5). Klein and Deforest (1963) reported that 5% phenol killed picornaviruses, but as much as 12% *o*-phenylphenol did not. On the other hand, Wright (1970*b*) found several substituted phenolics and cresylic acids to be effective against vesicular stomatitis virus. With the various formulations available in the United States and the lack of published data about efficacy, it is somewhat difficult to suggest uses for phenolics beyond noncritical and a few semicritical items. It is used as a disinfectant for decontamination purposes in laboratories.

Quaternary Ammonium Compounds

A variety of quaternary ammonium compounds, including benzalkonium chloride and cetylpyridinium chloride, have come into fairly wide usage since their introduction as germicides in 1935. As mentioned in Chapter 14, the mode of action of quaternary ammonium compounds appears to be associated with the agent's effect on the cytoplasmic membrane, which controls cell permeability. The quaternary ammonium compounds for many years were the most popular of all classes of disinfectants, primarily because of their blandness and low cost. In the laboratory, they appeared to be germicides with rapid action against test bacteria in vitro, particularly the staphylococci, but under ordinary conditions of use, their germicidal action is somewhat questionable. They are classed as low-level disinfectants with relatively poor activity against gram-negative bacteria. Indeed, commercial preparations containing ammonium acetate have been shown to support the growth of *Pseudomonas* species (Adair et al., 1969). Dixon et al. (1976) have discussed the problems associated with the use of antiseptics and disinfectants based on the quaternary compounds in the hospital environment and have described several outbreaks of disease associated with gram-negative bacterial contamination of quaternary ammonium solutions.

They have no tuberculocidal activity and, because of this, have a role in laboratory procedures for the isolation of tubercle bacilli from clinical materials (Wayne et al., 1962; Smithwick et al., 1975). Indeed, laboratory workers took advantage of the general ineffectiveness of quaternary ammonium compounds against various gram-negative bacteria, including *Pseudomonas* species (especially *P. aeruginosa*), in developing culture media that use quaternary ammonium compounds as selective factors against gram-positive organisms, allowing pseudomonads and some other gram-negative bacteria to grow. Klein and Deforest (1963) found that benzalkonium chloride has no activity against picornaviruses, even in 10% concentration. Because most quaternary ammonium compounds do not acquire intermediate-level activity at any usable concentration, they should not be used to disinfect critical medical items or most semicritical items.

These compounds are rapidly inactivated by contact with protein, cotton fibers, and other organic materials and gram-negative bacteria, such as *Pseudomonas*, Enterobacteriaceae, and *Serratia*, frequently have been noted to grow in them. They are good cleansing agents that can be used effectively for noncritical housekeeping purposes in the hospital and other health care settings.

Chlorine

Inorganic chlorine solutions in concentrations of 0.1 to 0.5% free chlorine are considered intermediate-level disinfectants and are among the best and most convenient germicides for spot disinfection. The mode of action of free chlorine, unlike that of free iodine, is considered to be the inactivation of sulfhydryl enzymes and protein denaturation, as well as inactivation of nucleic acids. Solutions of 1 to 5% (household bleach contains 3 to 5% sodium hypochlorite) are slightly sporicidal and fully tuberculocidal and inactivate vegetative bacteria. Klein and Deforest (1965) reported that all of 25 viruses, including the picornaviruses, were inactivated in 10 minutes by as little as 0.02% available chlorine.

Free chlorine, as derived from sodium hypochlorite or calcium hypochlorite, has limited use on medical devices in a hospital because of its corrosiveness. It can be used effectively in high concentration, however, as a spot disinfectant or for decontaminating spills, e.g., blood suspected of being positive for hepatitis B virus (Bond et al., 1977). It has been used as a disinfectant for hydrotherapy baths and in hemodialysis systems, but it has the disadvantage of being corrosive. Hypochlorite solutions cannot be left for long periods of time in a dialysis machine. The fact that they must be rinsed from the hemodialysis machine negates their efficacy overall because gram-negative bacteria in the rinsing water tend to grow in these systems in the absence of a disinfectant (Favero et al., 1975; Favero and Petersen, 1977).

Iodophors

Tinctures or iodophors of iodine have been used for many years by health professionals in infection control and for broader control purposes. Iodine (I_2) in its pure form is poorly soluble in water and is saturated at 0.03%, which is 300 ppm free iodine (free iodine being the chemical species I_2). Tinctures of iodine have been used primarily as antiseptic solutions, whereas iodophors are used as both antiseptics and disinfectants. Iodophors are the combination of iodine and a solubilizing agent or carrier in which the resulting complex or combination acts as a reservoir of iodine and liberates small amounts of free iodine when diluted with water. The number of carriers ranges from quaternary ammonium compounds, detergents, and others to polyvinylpyrrolidone (PVP or povidone).

Iodine is believed to function as a general cellular poison and to affect both nucleic acids and proteins. Some iodophors have been marketed as disinfectants and have the disadvantage of being unstable in the presence of hard water, heat, and organic soil, but they appear to be reliable, general-purpose disinfectants if used in concentrations recommended by the manufacturer. Some metallic instruments can be corroded if they are routinely disinfected with iodophors for long periods of time, but nonmetallic items seldom are damaged. Iodophor disinfectants traditionally are classified as low- to intermediate-level disinfectants, depending on concentration. As will be discussed, however, the concentration of the actual microbicidal agent, which is presumably free iodine, is usually unknown.

Formulations of iodophors usually list certain percentages of available iodine that have been used as indicators of germicidal potency. This does not appear to be correct. Many aspects related to the physical and organic chemistry of iodine complexes are not fully understood. For example, a povidone-iodine germicide formulated as an antiseptic usually contains 10% povidone-iodine and is said to yield 1% available iodine. The amount of free iodine present in these solutions has been reported to be approximately 1 ppm (Berkelman et al., 1981; Rodeheaver et al., 1976) and is controlled significantly by the amount of potassium iodide present as well as by the amount of water (see Chapter 8). Concentrated solutions of iodophor contain less free iodine in undiluted solutions than those that are diluted up to a point. Apparently, it is virtually impossible to chemically assay free iodine in the presence of complexed iodine without resorting to an extraction technique using solvents. Thus, one can readily appreciate that the manufacturer's direction for an iodophor disinfectant that calls for a 1:213 aqueous dilution of a concentrated product is designed to give the maximum degree of microbicidal efficiency, which probably correlates with the amount of free iodine present. There appears to be less free iodine in solution, or at least less microbicidal activity, when the product is diluted more or less than the prescribed 1:213 use-dilution.

Available iodine does not appear to be a sufficient indicator of potency for iodophor germicides. Berkelman and colleagues (1981), for example, reported the recovery of *Pseudomonas cepacia* from blood cultures of 52 patients in 4 hospitals in New York City over a 7-month period from April through October, 1980. Epidemiologic investigations indicated that the positive blood cultures were in fact pseudobacteremias, and the source of contamination was a commercially available 10% povidone-iodine solution that was used both as an antiseptic and a disinfectant. It was shown that *P. cepacia* gained entrance to blood culture tubes from povidone-iodine left on the skin prior to venipuncture or from povidone-iodine that was applied to blood culture bottle tops through which blood was inoculated by syringe into culture media. In addition, *P. cepacia* was isolated directly from the povidone-iodine solutions. This report is not the first to describe intrinsic microbial contamination of commercially available germicide solutions, but one would have thought that these solutions containing 1% available iodine would prevent survival of vegetative bacteria (or bacterial spores).

Unfortunately, most investigators tend to equate available iodine with free iodine. A review of the literature (see Chapter 8; Favero, 1982) concerning microbicidal capabilities of iodophor solutions reveals that virtually no researcher actually reports the amount of free iodine; rather, most express either a dilution of a particular formulation or, more often, amounts of available iodine in mg/L. This confusion may be due to equating the term "available iodine" with the term "available chlorine." The latter is defined as the amount of free (Cl_2 and HOCl) and combined chlorine (i.e., chloramines), both of which are microbicidal, although free chlorine is more active than combined chlorine. The term "available" when used with iodine means the amount that is titratable with sodium thiosulfate; available iodine as such is not microbicidal.

Available iodine can be thought of as an expression of the reservoir of complexed iodine that slowly releases free iodine in a given solution. As the free iodine is depleted, more free iodine instantaneously takes its place. For example, with an iodophor disinfectant that has 1% available iodine and 35 ppm free iodine, the free iodine that is inactivated by reacting with organic materials or bacteria is immediately replaced. Likewise, when it is titrated with sodium thiosulfate, the free iodine concentration is replaced instantaneously from the reservoir of available iodine (even though it is the free iodine that is being titrated); the end result is 1% or 10,000 ppm available iodine. The amount of *free* iodine, however, is much less, i.e., 35 ppm.

This does not alter the rationale for classifying iodophor disinfectants as intermediate-level disinfectants, but it does present a problem in defining use-concentration. Since it is complicated to assay for free iodine in the presence of iodophor solutions, and since it is current practice for manufacturers to include the amount of available iodine (whether accurate or not) on product labels as an implication of potency, I have elected to retain the use of available iodine as an indicator of potency for denoting strength in Table 25–2, but free iodine levels are listed also. It is emphasized that with iodophors, the manufacturer's directions are much more critical with respect to actual use-dilutions with water than most other disinfectants, and care should be taken to follow label instructions closely.

Alcohols

The value of alcohol as a surgical germicide has been reviewed by Spaulding (1964). Ethyl and isopropyl alcohols are rapidly bactericidal intermediate-level disinfectants and are remarkably active against the tubercle bacillus (Table 25–5). Neither ethanol nor isopropanol are sporicidal, and indeed, both alcohols are sometimes used to store clean spore crops of *Bacillus* and *Clostridium* species. They are fairly effective against all types of vegetative bacteria, but reports on the virucidal properties of alcohol are conflicting (Klein and Deforest, 1963; Wright, 1970a).

Alcohols characteristically evaporate quickly and leave no residue on treated surfaces, which may or may not be an advantage, depending on the item being disinfected. In some instances, they have been known to dissolve the lens mountings of certain types of optical instruments and, upon long exposure, tend to harden and swell plastic tubing, including polyethylene. Further, rubber articles absorb alcohol, and irritation to the skin or mucous membranes may follow. Alcohols in a concentration of 70% by volume may be a good choice for intermediate-level disinfection for some types of semi- and noncritical items.

Formaldehyde

Forty-percent formaldehyde gas dissolved in water constitutes a 100% solution of formalin; 8% formaldehyde in water is 20% formalin. Depending on its concentration, formaldehyde is classified as a high-level (8% formaldehyde plus 70% alcohol) or intermediate- to high-level (3 to 8% formaldehyde in water) disinfectant. Formaldehyde has a broad spectrum of action on microorganisms, and its mode of action is by alkylation with amino and sulfhydryl groups of proteins and ring nitrogen atoms of purine bases such as guanine (see Chapter 2) (Habeeb and Hiramoto, 1968). Their high sporicidal activities suggest that alkylation of nucleic acids may be more important in microbicidal action than changes in protein constituents. The action of formaldehyde on a protein coat of poliovirus progressively slows down the killing rate by obstructing penetration of the nucleic acid core (Gard, 1959). As mentioned previously, 8% formaldehyde in water is considered an intermediate- to high-level disinfectant; combining 8% formaldehyde in 65 to 70% isopropanol yields a compound that is rapidly bactericidal, tuberculocidal, and sporicidal, but the time required to achieve sterility using high numbers of spores as a challenge may be up to 18 hours or longer, depending on the test conditions (Spaulding, 1966).

Although these solutions of formaldehyde are considered to be intermediate- to high-level germicides, the irritating fumes of formaldehyde limit its usefulness in the hospital environment, and its toxicity for tissue requires that disinfected materials be rinsed thoroughly before use. Since it does not corrode equipment associated with hemodialysis systems, formaldehyde is currently considered the disinfectant of choice in a concentration of 1 to 2% (Favero et al., 1975) and is the germicide most commonly used to disinfect disposable hemodialyzers that are reused. In both instances, however, the problem of residual formaldehyde constitutes a potential health hazard to dialyzing patients, and hemodialysis systems and hemodialyzers must be thoroughly rinsed free of formaldehyde prior to use.

Glutaraldehyde

Glutaraldehyde is a saturated dialdehyde that is chemically related to formaldehyde and has been shown to be two to eight times more sporicidal than formaldehyde (Borick, 1968). Like formaldehyde, glutaraldehyde acts on microorganisms by alkylation, with amino and sulfhydryl groups of proteins and ring nitrogen atoms of purine bases. Disinfectants containing an aqueous solution of 2% glutaraldehyde are considered high-level disinfectants. When exposure times are in the range of 6 to 10 hours at room temperature, depending on the specific formulation, these disinfectants are approved by the EPA as sterilants.

Glutaraldehyde was used for many years as a disinfectant (Boucher, 1972). It was shown that alkaline preparations of glutaraldehyde are sporicidal (Pepper and Chandler, 1963; Borick, 1968). The microbicidal activity of aqueous glutaraldehyde appears to increase at alkaline pH; however, germicidal potency at high pH tends to decrease after storage and use of the disinfectant (Borick, 1968). Acidic preparations of glutaraldehyde can be sporicidal if the temperature is increased to 60° C; and microbicidal activity is increased by ultrasonic energy (Sierra and Boucher, 1971; Boucher, 1974). Other formulations combine glutaraldehyde and formaldehyde, and one is described as a buffered, phenol-glutaraldehyde solution that contains 2% glutaraldehyde and 7% phenol in a phenate buffering system. All of these preparations have been shown to be rapidly sporicidal; the glutaraldehyde-phenate buffering system was reported to be more sporicidal at room temperature than 2% alkaline glutaraldehyde (Pepper, 1980).

Two-percent glutaraldehyde solutions or some of the combinations mentioned previously are classified as high-level disinfectants when used in undiluted forms. These solutions have been approved by the EPA as sporicides and as disinfectants, with recommended contact times at room temperature of 10 to 20 minutes. The actual time in which high-level disinfection is accomplished cannot be based solely on the AOAC use-dilution test. Consequently, recommended times for disinfection will depend on the instrument being disinfected, the type and quantity of the microbiologic load, the amount of organic material and, most importantly, the results of in-use testing with the absence of vegetative bacteria used as a criterion. Most recommended exposure times are in the range of 10 to 30 minutes, and the Center for Disease Control has recently specified a contact time of 30 minutes to accomplish high-level disinfection of inhalation therapy equipment and endoscopic devices (CDC, 1981). Glutaraldehyde disinfectants are not as noxious, irritating to skin, or corrosive to certain types of critical patient care equipment as formaldehyde. Currently, glutaraldehyde-based disinfectants are those used most commonly to disinfect endoscopic equipment.

Hydrogen Peroxide

Hydrogen peroxide has been recognized as a germicide for more than a century. Application of low concentrations of unstable preparations to tissues containing inactivating levels of catalase, however, led to unfavorable results; this agent has been generally abandoned as an antiseptic. However, it has recently been used in stabilized form. Six-percent stabilized hydrogen peroxide is classified as a high-level disinfectant and has been shown to be sporicidal (see Chapter 11). Hydrogen peroxide has been shown to be bactericidal, virucidal (Mental and Schmidt, 1973), and (in high concentration) sporicidal (Toledo et al., 1971).The latter investigators obtained D values of 0.8 to 7.3 minutes at 24° C with both aerobic and anaerobic spore suspensions by using 10 to 25% hydrogen peroxide. Wardle and Renninger (1975) showed that 10^6 aerobic spores were inactivated at 25° C in 60 minutes with a 10% concentration of hydrogen peroxide. Hydrogen peroxide in concentrations of 3 to 6% appears to constitute a useful class of agents for disinfection of a variety of materials, including medical and surgical devices, and in concentrations of 6 to 25% shows promise as a chemosterilant.

Gaseous Disinfectants

These disinfectants include ethylene oxide, formaldehyde, and beta-propiolactone. All three are toxic to tissues, and because their microbicidal activity is subject to the same kinds of limitations as chemical germicides in general, they should be designated as disinfectants rather than as sterilizing agents. When used appropriately ethylene oxide has been shown to be a practical agent for producing sterility under controlled conditions, and only with ethylene oxide should the process be termed "gas sterilization." Indeed, ethylene oxide is the only one of the three that is used routinely in the United States to accomplish sterilization.

Ethylene oxide is used widely for disinfection and sterilization of instruments and equipment in hospitals and in the pharmaceutical industry. Ethylene oxide, like glutaraldehyde and formaldehyde, accomplishes alkalinization of protein as its mode of action in inactivating microorganisms. Ethylene oxide is considered a high-level disinfectant and, at appropriate concentrations, i.e., 450 to 800 mg/L, exposure times, and humidities, can be used for sterilization of heat-labile articles. A number of commercial devices are available, and this sophisticated equipment is designed to control for the critical variables of prehumidification, temperature, humidity, and ethylene oxide concentration.

Ethylene oxide tends to become absorbed in certain types of materials, and it is necessary to subject exposed materials to a period of deaeration to remove residual ethylene oxide. Since the prehumidification and relative humidity of the gas mixture within commercial gas sterilizers have been shown to be critical, such tolerances virtually negate the use of ethylene oxide in a home-made type of apparatus as was used by some investigators in the 1940s and 1950s. Ethylene oxide gas is toxic, mutagenic, carcinogenic, and irritating to eyes and mucous membranes. Because it is highly penetrating, this gas can leave a residue that must be removed by mechanical ventilation. Ethylene oxide is used routinely in hospitals for the sterilization of heat-labile surgical and medical devices; the effectiveness of the process is usually monitored with biologic indicators as well as physical parameters on the individual sterilizer. Refer to Chapter 2 for a more detailed discussion.

Formaldehyde gas has been used for decontamination and as a disinfectant in formaldehyde chambers. The bactericidal effect is variable, however, and depends significantly on the relative humidity being at 70% or more, which unfortunately promotes corrosion of metals. Formaldehyde fumes are irritating, and the gas penetrates porous materials poorly compared to ethylene oxide. Formaldehyde vapor has been used to sterilize respiratory care equipment, and some techniques have been described by Sykes (1972), who pointed out that sterilization could be achieved in 2 hours by circulation of the vapor through a closed circuit. The formaldehyde gas had to be neutralized with ammonia gas, however, and the machine had to be cycled in a well ventilated room for at least 8 to 24 hours to dissipate all toxic vapors. Because of the time involved and the irritating nature of the gas, this procedure is not used routinely in hospitals in the United States.

Beta-propiolactone has been used as a vapor-phase disinfectant and was found by Hoffman and Warshowsky (1958) to be a more effective sporicide than ethylene oxide. Allen and Murphy (1960) successfully used it for instrument disinfection. Concentration control and side effects make this gas unsuitable for the disinfection of instruments and equipment on a routine basis in the hospital environment in the United States.

EVALUATION OF ACTUAL GERMICIDAL EFFECTIVENESS

Two basic types of evaluation procedures can be used to compare the microbicidal efficiency of various chemical germicides. First, laboratory tests, using a known number of microorganisms, can be performed to determine (1) the time needed to achieve disinfection for given concentrations of a chemical germicide or a particular procedure, or (2) the concentration of a germicide needed to produce a desired disinfection time. The second type of test involves evaluation of a chemical germicide by an actual or simulated in-use test along with an appropriate microbiologic assay. Depending on the test organisms used, the results can indicate the level of capabilities of a disinfection procedure. Such tests are performed with or without added organic loads.

In the United States, the basic laboratory tests for the evaluation of chemical germicides used by the EPA as well as by scientific investigators have been described by the AOAC (1970). The AOAC use-dilution method involves testing pure cultures of microorganisms that are dried either on surgical threads or in small porcelain cups against a specific chemical germicide at a controlled contact time and temperature, usually 10 minutes at 20° C. It is designed as a dry test (i.e., the inoculum is placed in a receptacle and dried prior to exposure to the germicide). When 10^5 to 10^6 bacterial spores per test vehicle are used, such a test constitutes a fairly stringent challenge. With the dried inoculum, it is fairly difficult for chemical germicides to penetrate to such an extent that the entire population is killed. The assay procedure is based on growth or no growth of surviving microorganisms after exposure of a specific number of carriers. If the test is designed as a sporicidal test, by definition, it involves complete kill of 10^5 to 10^6 dried bacterial spores of *Bacillus subtilis* or *Clostridium sporogenes*. As mentioned previously, this constitutes a severe challenge that could be exceeded only by the use of naturally occurring spores, for example, those in the soil (Bond et al., 1970) or those embedded in dried organic material. Consequently, one can usually be assured that a chemical germicide that has been tested and approved by the EPA for use as a sporicide is an effective chemical sterilant if it is stored and used properly. Obviously, problems associated with misuse or improper preparation (i.e., improper cleaning of an instrument) can contribute to the failure of a sterilization or high-level disinfection procedure.

The AOAC use-dilution test applied to vegetative bacteria is somewhat less reliable. The test as a whole enables the EPA and manufacturers to provide a minimum set of guidelines for comparing and judging the activity of germicidal products. However, this test does not constitute as severe a challenge with vegetative bacteria as it does with bacterial spores. First, the factors influencing microbial resistance to germicides, mentioned in a previous section, are greatly magnified when vegetative bacteria are involved. If the germicide is stored under the wrong conditions or mixed improperly, or if the item to be disinfected is not properly cleaned, the probability is great that the intended level of disinfection, whether it be high, intermediate, or low, will fail to be reached. Furthermore, the number and type of species of bacteria that are used are limited. More importantly, they are pure cultures that have been subcultured for years and maintained in laboratories. That difference in itself will give a false sense of security, because microorganisms in their naturally occurring state tend to be significantly more resistant to physical and chemical stresses than when they are subcultured (Carson et al., 1972, 1978; Favero et al., 1975). Hence, although this test may provide the EPA, manufacturers, and investigators with a somewhat standardized basis for maintaining minimum criteria for comparing germicides, it cannot be used as the sole criterion for selecting chemical germicides to accomplish specific degrees of disinfection, whether it be complete sterilization or high- to low-level disinfection. This is especially true in the hospital environment.

Of great importance in the hospital environment is the manner in which the instrument or item is used, as well as the anticipated risk of disease transmission. In most instances it is not necessary for most hospital laboratories to test the antimicrobial effectiveness of commercial products unless such testing is part of a well designed research or evaluation project. Instead, one may rely on the testing performed or validated by the EPA for disinfectant agents. It is a fairly safe assumption that any chemical germicide registered with the EPA meets minimum test criteria. In addition, with certain types of instruments or medical devices, procedures are published in the literature on certain generic chemical germicides, along with suggested contact times (CDC, 1981). There are times, however, when the use of a particular device or item is new or unique, when the intended germicide has not been used previously in a specific manner, or when the germicide is new. In these cases, one may wish to do an in-use test. These tests should be well designed and can be conducted in one of two general ways.

The first type of in-use test is one in which the item is microbiologically assayed after it has been contaminated in actual use and after an appropriate germicidal treatment has been done. The type of microbiologic assay would depend on the intended outcome, i.e., sterilization or disinfection. For example, if the intended disinfectant level for a medical device were high, the microbiologic criterion would be the absence of vegetative bacteria, but not necessarily of bacterial spores. Although this type of testing can be valuable, it is rather cumbersome, and few laboratories have the resources to do this type of testing on a routine basis. It is emphasized that this type of microbiologic testing is designed as part of a research project and should not be incorporated into a program of routine microbiologic monitoring (Favero, 1980).

Another type of in-use test is to operate the medical device or instrument (e.g., a hemodialysis machine) in the laboratory and provide a microbiologic challenge, either by inoculation of naturally occurring microorganisms or with pure cultures, and perform the disinfection procedure. The microbiologic criterion would not change with respect to culture assays, but certain critical variables such as temperature and exact verified germicide concentrations could be controlled.

Regardless of whether one or both types of the in-use tests just described are performed, the contact times invariably are much longer than the 10 minutes employed in the AOAC use-dilution test. For example, most commercially available high-level disinfectants, such as 2% aqueous glutaraldehyde and related germicides, have been approved for disinfection with a contact time of 10 minutes at room temperature. Under actual conditions of use, however, this amount of time may not be sufficient to fully accomplish high-level disinfection, i.e., killing of all contaminating vegetative bacteria, including mycobacteria, but not bacterial endospores. Consequently, contact times of 20 to 30 minutes have been found to be more appropriate (Mackel, 1974; CDC, 1981; APHA, 1978). Several studies (House and Henderson, 1965; Pierce et al., 1970) underscore the need for in-use testing of naturally contaminated equipment to establish more reliable contact times than those achieved with AOAC tests.

It is clear, then, that the actual effectiveness of a chemical germicide is influenced only in part by the nature of the active agent. Of equal and perhaps greater importance is the way in which it is used in the hospital. Many disinfectants, especially the low- and intermediate-level disinfectants, have little margin of safety, and misuse may lead to germicidal failure. Consequently, there is always a tendency for a hospital's infection control personnel to decide to use microbiologic cultures in a limited program to monitor the effectiveness of disinfection and sterilization. It should be emphasized most strongly that routine or widespread environmental culturing is generally discouraged because it offers little data of use to infection control personnel.

Moreover, any environmental monitoring program must be well designed with a specific objective in mind (Favero, 1980). It makes little sense, for example, to evaluate items or areas that are unlikely to play a role in disease transmission. Although floors or furniture and other noncritical items are cleaned and disinfected, they should not be tested, even to evaluate the effectiveness of hospital housekeeping personnel; a clean white glove has been said to be a more effective testing tool than a culture plate in these areas. To the extent that it is used, microbiologic monitoring should be limited to high-risk (critical or semicritical) items. Even then, microbiologic monitoring should not take the place of scrupulous attention to the actual performance of the sterilization or disinfection procedures.

STRATEGIES FOR MONITORING CHEMICAL DISINFECTION OF CRITICAL PATIENT CARE EQUIPMENT

Respiratory Therapy and Anesthesia Breathing Circuits

The most important part of an environmental control program to reduce infections transmitted directly or indirectly by respiratory therapy and anesthesia equipment breathing circuits is the use of proper cleaning and disinfection procedures. The most efficient and cost-effective way to accomplish these goals is to sterilize these devices with steam under pressure or ethylene oxide. If this is not possible, the *minimum* procedure that should be used is one that achieves high-level disinfection. In this case, these items may be spot-checked every few months or when disinfection or usage procedures change. Routine or scheduled bacteriologic testing is not required. Although there is no adequate microbiologic guideline for this strategy that is supported by epidemiologic studies, the most widely used criterion of acceptability is the absence of vegetative bacteria on components of the breathing circuits after the disinfection process (Mackel, 1974; APHA, 1978; Favero, 1980).

Hemodialysis Systems

Gram-negative water bacteria can multiply relatively fast in fluids associated with hemodialysis systems such as distilled, softened, deionized, and reverse-osmosis water, as well as in the dialysis fluid itself. Although these fluids do not need to be sterile, excessive levels of gram-negative bacterial contamination pose a risk of pyrogenic reactions and septicemia. A quantitative microbiologic guideline for levels of contamination has been proposed (AAMI, 1974; Favero and Petersen, 1977).

It is suggested that dialysis fluids and water used to prepare dialysis fluids be checked microbiologically at least once a month. Microbiologic guidelines for these procedures include sampling the water used to prepare dialysis fluid at that point at which it is mixed with concentrated dialysis fluid. The level of bacterial contamination should not exceed 200 cells per ml. Dialysis fluid should be sampled at the end of a dialysis treatment, and the level of bacterial contamination should not exceed 2000 cells per ml. In both instances, routine standard plate count or membrane filter assay procedures with appropriate culture media, such as trypticase soy agar or plate count agar, can be used. Hemodialysis systems are among the few medical devices for which periodic microbiologic assays are recommended and for which the few microbiologic quantitative guidelines are actually based on epidemiologic studies (Favero and Petersen, 1977; Favero et al., 1975).

Arterial Pressure Transducers

Arterial pressure transducers have been incriminated in disease transmission, and the best means of control are adequate cleaning and sterilization, as well as proper placement. Scheduled microbiologic sampling is not required, but these items should then be assayed occasionally to determine whether they are being used properly. The criterion of acceptability is sterility.

Endoscopic Equipment

In recent years, a number of flexible and rigid endoscopic devices have been designed for use on patients. These devices have the advantage, in many cases, of eliminating surgical procedures, but since they touch mucous membranes or are placed into normally sterile areas of the body, they are in the category of semicritical to critical items. Preferably, all endoscopes, including flexible fiberoptic endoscopes, should be cleaned appropriately and submitted to a sterilization procedure. There are instances, however, in which either this is not routinely feasible or the state of the art is such that procedures less extensive than sterilization are employed. In these instances, the absolute minimum strategy should be the use of meticulous cleaning and high-level disinfection (Ad Hoc Committee on Infection Control, 1978, 1980; Bond et al., 1979; CDC, 1981). A variety of chemical germicides are classified as high-level disinfectants already have been discussed. When selecting a germicide for use with lensed instruments, however, one must consider not so much the activity of the germicide as the compatibility after extended use with the instrument. Currently, the high-level disinfectants used most widely with endoscopic equipment are ethylene oxide and 2% glutaraldehyde-based germicides. As with other critical and semicritical items, the best way to ensure actual success of the disinfection procedure is to adhere strictly to established cleaning and disinfection protocols. Scheduled microbiologic sampling is not required, but if it is done periodically, the criterion of acceptability is the absence of vegetative bacteria.

Miscellaneous Procedures and Equipment

Numerous items and patient care equipment pose varying degrees of infection risk associated with their use. They may directly contact skin and mucous membranes of body orifices or the peritoneal cavity, but usually not deep tissue. Items in this category, in addition to flexible fiberoptic and endoscope equipment, include hydrotherapy equipment, antiseptic solutions, nonsterile solutions prepared in the hospital, and hemodialyzers. With these items, as with others mentioned previously, the most important element in environmental control is not microbiologic sampling, but rather adherence to tested protocols associated with their cleaning, preparation, disinfection or sterilization, length of use, and maintenance. Even spot-checking these items and procedures is not recommended in most cases because of the absence of meaningful microbiologic guidelines supported by epidemiologic criteria. One arbitrary guideline that can be used is the absence of recognized pathogens after a particular cleansing and disinfection procedure, which can be interpreted, from a realistic standpoint, as the absence of vegetative bacteria.

Unnecessary Microbiologic Assays

There are a number of items and procedures in the hospital and other health care environments for which microbiologic sampling on either a scheduled or periodic basis is neither cost effective nor rational. These include sterile intravenous solutions, injectable solutions, disposable syringes, disposable blood lines, artificial kidneys (even those that are reused), and all other items that are received in a sterile state. Equipment and solutions sterilized within the hospitals need not be sampled microbiologically. Instead, quality assurance testing associated with sterilization procedures, such as appropriate biologic indicator spores (Favero, 1980), should be used to ensure that the sterilization process per se is performing to specifications and that the associated personnel practices are being performed correctly.

It is recognized that inanimate surfaces and air associated with critical areas such as surgical suites and intensive care areas may contain reservoirs of microorganisms. However, the chance for disease transmission in environments that are adequately cleaned and maintained is remote. Environmental control procedures associated with housekeeping and engineering services should adhere to testing cleaning, disinfection, and maintenance protocols. Therefore, microbiologic sampling on either a scheduled or periodic basis should not be done on floors, walls, intramural air, or other inanimate environmental surfaces. Conversely, appropriate sampling should be done when a disease outbreak appears to be associated with a certain part of the environment, such as the air ventilation system (Favero, 1980; CDC, 1981).

Environmental Microbiologic Sampling During Outbreaks of Disease

The strategy that should be used during an outbreak of disease with respect to environmental microbiologic sampling depends on several factors. First, the epidemiologist must determine whether certain procedures, equipment, instruments, or other parts of the environment may be playing a direct or indirect role in the outbreak. An outbreak of nosocomial disease does not mean automatically that environmental microbiologic sampling at any level is required. Second, if environmental microbiologic sampling is believed necessary, the microbiologist and epidemiologist should coordinate the sampling scheme and determine the procedures, items, or parts of the environment that require microbiologic assay.

The application of a microbiologic guideline in this context differs from one that is associated with scheduled or periodic sampling. During the investigation of an outbreak of nosocomial infection, environmental testing is usually directed towards the specific pathogenic microorganism. Consequently, if the outbreak is due to *Pseudomonas aeruginosa*, this organism is sought in the various environmental items that are sampled. In this respect, the guideline tends to be more qualitative than quantitative, although in some instances one must rely on established guidelines. For example, if there is an outbreak of pyrogenic reactions in a hemodialysis center, one would rely on established guidelines (AAMI, 1974; Favero and Petersen, 1977). If water or ice in a hospital is incriminated in an outbreak of nosocomial salmonellosis, assays should be used for determining fecal coliform bacteria, and the total number of microorganisms, in addition to a selective assay for salmonellae. Thus, the microbiologic guideline here is flexible and basically determined by the nature of the disease outbreak.

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GUIDELINE FOR HANDWASHING AND HOSPITAL ENVIRONMENTAL CONTROL, 1985

Supersedes Guideline for Hospital Environmental Control
Published in 1981

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RANKING SCHEME FOR RECOMMENDATIONS

CATEGORY I

Measures in Category I are strongly supported by well-designed and controlled clinical studies that show their effectiveness in reducing the risk of nosocomial infections, or are viewed as effective by a majority of expert reviewers. Measures in this category are viewed as applicable for most hospitals—regardless of size, patient population, or endemic nosocomial infection rates.

CATEGORY II

Measures in Category II are supported by highly suggestive clinical studies in general hospitals or by definitive studies in specialty hospitals that might not be representative of general hospitals. Measures that have not been adequately studied but have a logical or strong theoretical rationale indicating probable effectiveness are included in this category. Category II recommendations are viewed as practical to implement in most hospitals.

CATEGORY III

Measures in Category III have been proposed by some investigators, authorities, or organizations, but, to date, lack supporting data, a strong theoretical rationale, or an indication that the benefits expected from them are cost effective. Thus, they are considered important issues to be studied. They might be considered by some hospitals for implementation, especially if the hospitals have specific nosocomial infection problems, but they are *not* generally recommended for widespread adoption.

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Preface

In 1980, the Centers for Disease Control (CDC) began developing a series of guidelines entitled *Guidelines for the Prevention and Control of Nosocomial Infections.* The purpose of the *Guidelines* was twofold: 1) to disseminate advice on how to prevent or control specific nosocomial infection problems and 2) to cover the questions most frequently asked of the Hospital Infections Program staff on different aspects of the hospital's inanimate environment *(1).* One of the first *Guidelines* to be published was the *Guideline for Hospital Environmental Control.* It was written by Bryan P. Simmons, M.D. in consultation with Thomas M. Hooton, M.D., and George F. Mallison, M.P.H., and in collaboration with a working group consisting of Edward J. Bertz; Mary K. Bruch; Sue Crow, R.N., M.S.N.; William E. Scheckler, M.D.; Harold Laufman, M.D., Ph.D.; Janet K. Schultz, R.N., M.S.N.; Earle H. Spaulding, Ph.D.; and Richard P. Wenzel, M.D.

In February 1981, CDC mailed to each U. S. acute-care hospital Part I of the *Guideline for Hospital Environmental Control,* which contained sections entitled "Antiseptics, Handwashing, and Handwashing Facilities," "Cleaning, Disinfection, and Sterilization of Hospital Equipment," and "Microbiologic Surveillance of the Environment and of Personnel in the Hospital." In October 1981, Part II of the *Guideline for Hospital Environmental Control,* which contained the sections "Housekeeping Services and Waste Disposal," "Laundry Services," "Intensive Care Units," and "Pharmacy," was published. In July 1982, the section on "Cleaning, Disinfection, and Sterilization of Hospital Equipment" was revised. In November 1982, the two parts of the *Guideline* were combined into a single document entitled *Guideline for Hospital Environmental Control,* and copies were mailed to all U.S. acute-care hospitals.

In October 1983, CDC issued a statement entitled "Clarification of Guideline Recommendations on Generic Antiseptic, Disinfectant, and Other Products," which was mailed to all U.S. acute-care hospitals. The statement emphasized that CDC recommendations are not intended to endorse any particular commercial product or to exclude the use of other commercial products containing generic ingredients not mentioned in the *Guideline for Hospital Environmental Control.*

In November 1983, a follow-up statement requested that users delete the portion of the *Guideline for Hospital Environmental Control* that recommended specific generic antimicrobial ingredients for use in health care personnel handwashes and announced that the entire *Guideline* would be comprehensively revised. In June 1984, a draft of the proposed revision was mailed to 150 scientists and infection control professionals for review and comment. Rather than using an expert working group to finalize the content of this *Guideline,* we used the written comments and suggestions which we received from the reviewers to determine the final content of the *Guideline* and the ranking of the recommendations.

This *Guideline* incorporates the above revisions, as well as newly available information; the title has been changed to *Guideline for Handwashing and Hospital Environmental Control.* It replaces all previous handwashing and environmental control statements issued or published by the Hospital Infections Program, Center for Infectious Diseases, CDC.

MAJOR CHANGES IN THE GUIDELINE

Since this *Guideline* contains many important changes from the original *Guideline for Hospital Environmental Control,* it is important that users read the entire *Guideline* carefully. The major changes in the titles and content of sections are listed below:

1. The section "Handwashing," which replaces the old section entitled "Antiseptics, Handwashing, and Handwashing Facilities," contains updated recommendations for handwashing with plain soaps or detergents and with antimicrobial-containing products. Rather than recommending specific generic ingredients for handwashing with antimicrobial-containing products, the *Guideline* indicates that hospitals may choose from appropriate products in categories defined by the U.S. Food and Drug Administration (FDA), since preparations used to inhibit or kill microorganisms on skin are categorized by an FDA advisory review panel for nonprescription (over-the-counter [OTC]) antimicrobial drug products *(2).* Manufacturers of antimicrobial-containing products voluntarily submit data to the review panel, which categorizes the products according to their intended use, i.e., antimicrobial soaps, health-care personnel handwashes, patient preoperative skin preparations, skin antiseptics, skin wound cleansers, skin wound protectants, and surgical hand scrubs. Generic antimicrobials for each use category are further divided: Category I (safe and efficacious); Category II (not safe and/or efficacious); and Category III (insufficient data to categorize). Consequently, chemical germicides formulated as antiseptics are categorized by the FDA into groupings by use and efficacy, but they are not regulated or registered in the same fashion as chemical germicides are by the U.S. Environmental Protection Agency (EPA).

   Persons responsible for selecting commercially marketed health-care-personnel handwashes can obtain information about categorization of products from the Center for Drugs and Biologics, Division of OTC Drug Evaluation, FDA, 5600 Fishers Lane, Rockville, MD 20857. In addition, information published in the scientific literature, presented at scientific meetings, documented by manufacturers, and obtained from other sources deemed important may be considered.
2. The section "Cleaning, Disinfecting, and Sterilizing of Patient-Care Equipment" has been rewritten. Medical devices, equipment, and materials are divided into three categories (critical, semicritical,

and noncritical) based on the risk of infection involved in their use. Revised recommendations for sterilizing and disinfecting items in these categories are included in this section. Rather than listing specific chemical germicides, the *Guideline* indicates that hospitals may choose from sterilant and disinfectant formulations registered with the EPA, since chemical germicides are regulated and registered by the EPA *(3)*. Manufacturers of chemical germicides formulated as general disinfectants, hospital disinfectants, and disinfectants used in other environments, such as the food industry, are required by EPA to test their formulations using specific protocols for microbicidal efficiency, stability, and toxicity to humans. In past years, the EPA has reserved the right to test and verify formulations of chemical germicides for their specified efficacy; however, in practice only those formulations to be registered as sterilants or sporicides were actually tested. In 1982, the EPA discontinued this testing. Currently, formulations of chemical germicides are registered by the EPA based on data obtained from the manufacturer.

Persons responsible for selecting chemical germicides should keep in mind that the field is highly competitive, and exaggerated claims are often made about the germicidal efficiency of specific formulations. When questions regarding specific claims or use arise, the Disinfectants Branch, Registration Division, Office of Pesticides, EPA, 401 M Street, S.W., Washington, D.C. 20460, can be consulted. As with handwashing products, information in the scientific literature, presented at scientific meetings, documented by manufacturers, and obtained from other sources deemed important may be considered.

The recommendation against reprocessing and reusing single-use items has been removed. Since there is lack of evidence indicating increased risk of nosocomial infections associated with the reuse of *all* single-use items, a categorical recommendation against *all* types of reuse was not considered justifiable. Rather than recommending for or against reprocessing and reusing single-use items, the *Guideline* indicates that items or devices that cannot be cleaned and sterilized or disinfected without altering their physical integrity and function should not be reprocessed. In addition, reprocessing procedures that result in residual toxicity or compromise the overall safety or effectiveness of the items or devices should be avoided. Arguments for and against reprocessing and reusing single-use items have been summarized in a report from the International Conference on the Reuse of Disposable Medical Devices in the 1980's *(4)*.

3. The section "Microbiologic Sampling" replaces the old section entitled "Microbiologic Surveillance of the Environment and of Personnel in the Hospital." The recommendation for microbiologic sampling of infant formulas prepared in the hospital has been removed, since there is no epidemiologic evidence to show that such sampling reduces the infection rate in hospitals. Information and recommendations for microbiologic surveillance of personnel have been deleted, since this topic is addressed in the *Guideline for Infection Control in Hospital Personnel (5)*.
4. A new section, "Infective Waste," has been added. It contains information about identifying infective waste and recommendations for its handling and disposal.
5. The section "Housekeeping" replaces the old section "Housekeeping Services and Waste Disposal." Recommendations against use of carpets in patient-care areas have been removed, since there is no epidemiologic evidence to show that carpets influence the nosocomial infection rate in hospitals *(6)*; whether to use carpets, therefore, is not considered an infection control issue.
6. The section "Laundry" contains a discussion of and recommendations for both hot-water and reduced-temperature washing.
7. The section "Intensive Care Units" has been deleted, since it primarily dealt with information and recommendations that are covered elsewhere in this *Guideline* and in the *Guideline for Isolation Precautions in Hospitals (7)*.
8. The section "Pharmacy" has been deleted from this *Guideline*, since it primarily dealt with recommendations for admixture of parenteral fluids that are contained in the *Guideline for Prevention of Intravascular Infections*.

The recommendations presented in this *Guideline* were chosen primarily for their acknowledged importance to infection control, but other factors, such as the feasibility of implementing them and their potential costs to hospitals, were also considered. Many recommendations are intended to reduce or eliminate expensive practices that are not likely to prevent infections. Some of the recommendations are based on well-documented epidemiologic studies; others are based on a reasonable theoretical rationale, since for many of these practices little or no scientifically valid evidence is available to permit evaluation of their effect on the incidence of infection. Because new studies are constantly revealing pertinent information in this field, users of this *Guideline* should keep informed of other sources. The recommendations presented in this *Guideline* may be modified as necessary for an individual hospital and are not meant to restrict a hospital from developing recommendations that may be more appropriate to its own unique needs. The recommendations have no force of law or regulation.

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Section 1: Handwashing

INTRODUCTION

Handwashing is the single most important procedure for preventing nosocomial infections. Handwashing is defined as a vigorous, brief rubbing together of all surfaces of lathered hands, followed by rinsing under a stream of water. Although various products are available, handwashing can be classified simply by whether plain soap or detergents or antimicrobial-containing products are used *(1)*. Handwashing with plain soaps or detergents (in bar, granule, leaflet, or liquid form) suspends microorganisms and allows them to be rinsed off; this process is often referred to as mechanical removal of microorganisms. In addition, handwashing with antimicrobial-containing products kills or inhibits the growth of microorganisms; this process is often referred to as chemical removal of microorganisms. Routine handwashing is discussed in this *Guideline*; the surgical hand scrub is discussed in the *Guideline for Prevention of Surgical Wound Infections*.

EPIDEMIOLOGY

The microbial flora of the skin consists of resident and transient microorganisms; the resident microorganisms survive and multiply on the skin and can be repeatedly cultured, while the transient microbial flora represent recent contaminants that can survive only a limited period of time. Most resident microorganisms are found in superficial skin layers, but about 10%-20% can inhabit deep epidermal layers *(2,3)*. Handwashing with plain soaps and detergents is effective in removing many transient microbial flora *(4-6)*. Resident microorganisms in the deep layers may not be removed by handwashing with plain soaps and detergents, but usually can be killed or inhibited by handwashing with products that contain antimicrobial ingredients.

Many resident skin microorganisms are not highly virulent and are not implicated in infections other than skin infections. However, some of these microorganisms can cause infections in patients when surgery or other invasive procedures allow them to enter deep tissues or when a patient is severely immunocompromised or has an implanted device, such as a heart valve. In contrast, the transient microorganisms often found on the hands of hospital personnel can be pathogens acquired from colonized or infected patients and may cause nosocomial infections. Several recent studies have shown that transient and resident hand carriage of aerobic gram-negative microorganisms by hospital personnel may be more frequent than previously thought *(7-10)*. More study on the bacteriology of hands is needed to fully understand the factors that contribute to persistent hand carriage of such microorganisms *(11)*.

CONTROL MEASURES

The absolute indications for and the ideal frequency of handwashing are generally not known because of the lack of well-controlled studies. Listing all circumstances that may require handwashing would be a lengthy and arbitrary task. The indications for handwashing probably depend on the type, intensity, duration, and sequence of activity. Generally, superficial contact with a source not suspected of being contaminated, such as touching an object not visibly soiled or taking a blood pressure, does not require handwashing. In contrast, prolonged and intense contact with any patient should probably be followed by handwashing. In addition, handwashing is indicated *before* performing invasive procedures, *before* taking care of particularly susceptible patients, such as those who are severely immunocompromised or newborn infants, and *before* and *after* touching wounds. Moreover, handwashing is indicated, even when gloves are used, *after* situations during which microbial contamination of the hands is likely to occur, especially those involving contact with mucous membranes, blood and body fluids, and secretions or excretions, and *after* touching inanimate sources that are likely to be contaminated, such as urine-measuring devices. In addition, handwashing is an important component of the personal hygiene of all hospital personnel, and *handwashing should be encouraged when personnel are in doubt about the necessity for doing so.*

The circumstances that require handwashing are frequently found in high-risk units, because patients in these units are often infected or colonized with virulent or multiply-resistant microorganisms, and are highly susceptible to infection because of wounds, invasive procedures, or diminished immune function. Handwashing in these units is indicated between direct contact with different patients and often is indicated more than once in the care of one patient, for example, after touching excretions or secretions, before going on to another care activity for the same patient.

The recommended handwashing technique depends on the purpose of the handwashing. The ideal duration of handwashing is not known, but washing times of 15 seconds *(6)* or less *(5)* have been reported as effective in removing most transient contaminants from the skin. Therefore, for most activities, a vigorous, brief (at least 10 seconds) rubbing together of all surfaces of lathered hands followed by rinsing under a stream of water is recommended. If hands are visibly soiled, more time may be required for handwashing.

The absolute indications for handwashing with plain soaps and detergents versus handwashing with antimicrobial-containing products are not known because of the lack of well-controlled studies comparing infection rates when such products are used. For most routine activities, handwashing with plain soap appears to be sufficient, since soap will allow most transient microorganisms to be washed off *(4-6)*.

Handwashing products for use in hospitals are available in several forms. It is important, however, that the product selected for use be acceptable to the personnel who will use it *(6)*. When plain soap is selected for handwashing, the bar, liquid, granule, or soap-impregnated tissue form may be used. It is preferable that bar soaps be placed on racks that allow water to drain. Since liquid-soap containers can become contaminated and might serve as reservoirs of microorganisms, reusable liquid containers need to be cleaned when empty and refilled with fresh soap. Completely disposable containers obviate the need to empty and clean dispensers but may be more expensive. Most antimicrobial-containing handwashing products are available as liquids. Antimicrobial-containing foams and rinses are also available for use in areas without easy access to sinks.

In addition to handwashing, personnel may often wear gloves as an extra margin of safety. As with handwashing, the absolute indications for wearing gloves are not known. There is general agreement that wearing sterile gloves is indicated when certain invasive procedures are performed or when open wounds are touched. Nonsterile gloves can be worn when hands are likely to become contaminated with potentially infective material such as blood, body fluids, or secretions, since it is often not known which patients' blood, body fluids, or secretions contain hepatitis B virus or other pathogens. Further, gloves can be worn to prevent gross microbial contamination of hands, such as when objects soiled with feces are handled. When gloves are worn, handwashing is also recommended because gloves may become perforated during use and because bacteria can multiply rapidly on gloved hands.

The convenient placement of sinks, handwashing products, and paper towels is often suggested as a means of encouraging frequent and appropriate handwashing. Sinks with faucets that can be turned off by means other than the hands (e.g., foot pedals) and sinks that minimize splash can help personnel avoid immediate recontamination of washed hands.

Although handwashing is considered the most important single procedure for preventing nosocomial infections, two reports showed poor compliance with handwashing protocols by personnel in medical intensive care units, especially by physicians *(12)* and personnel taking care of patients on isolation precautions *(13)*. Failure to wash hands is a complex problem that may be caused by lack of motivation or lack of knowledge about the importance of handwashing. It may also be caused by obstacles such as understaffing, inconveniently located sinks, absence of paper towels, an unacceptable handwashing product, or the presence of dermatitis caused by previous handwashing. More study is needed to identify which of these factors, alone or in combination, contribute significantly to the problem of poor compliance with handwashing recommendations.

RECOMMENDATIONS

1. Handwashing Indications

a. In the absence of a true emergency, personnel should *always* wash their hands
    1) **before** performing invasive procedures; *Category I*
    2) **before** taking care of particularly susceptible patients, such as those who are severely immunocompromised and newborns; *Category I*
    3) **before** and **after** touching wounds, whether surgical, traumatic, or associated with an invasive device; *Category I*
    4) **after** situations during which microbial contamination of hands is likely to occur, especially those involving contact with mucous membranes, blood or body fluids, secretions, or excretions; *Category I*
    5) **after** touching inanimate sources that are likely to be contaminated with virulent or epidemiologically important microorganisms; these sources include urine-measuring devices or secretion-collection apparatuses; *Category I*
    6) **after** taking care of an infected patient or one who is likely to be colonized with microorganisms of special clinical or epidemiologic significance, for example, multiply-resistant bacteria; *Category I*
    7) **between** contacts with different patients in high-risk units. *Category I*

b. Most routine, brief patient-care activities involving *direct* patient contact other than that discussed in 1.a. above, e.g., taking a blood pressure, do not require handwashing. *Category II.*

c. Most routine hospital activities involving indirect patient contact, e.g., handing a patient medications, food, or other objects, do not require handwashing. *Category I.*

2. Handwashing Technique

For routine handwashing, a vigorous rubbing together of all surfaces of lathered hands for at least 10 seconds, followed by thorough rinsing under a stream of water, is recommended. *Category I*

3. Handwashing with Plain Soap

a. Plain soap should be used for handwashing unless otherwise indicated. *Category II*

b. If bar soap is used, it should be kept on racks that allow drainage of water. *Category II*

c. If liquid soap is used, the dispenser should be replaced or cleaned and filled with fresh product when empty; liquids should not be added to a partially full dispenser. *Category II*

4. Handwashing with Antimicrobial-Containing Products (Health-Care Personnel Handwashes)

a. Antimicrobial handwashing products should be used for handwashing before personnel care for newborns and when otherwise indicated during their care, between patients in high-risk units, and before personnel take care of severely immunocompromised patients. *Category III* (Hospitals may choose from products in the product category defined by the FDA as health-care personnel handwashes. Persons responsible for selecting commercially marketed antimicrobial health-care personnel handwashes can obtain information about categorization of products from the Center for Drugs and Biologics, Division of OTC Drug Evaluation, FDA, 5600 Fishers Lane, Rockville, MD 20857. In addition, information published in the scientific literature, presented at scientific meetings, documented by manufacturers, and obtained from other sources deemed important may be considered.)

b. Antimicrobial-containing products that do not require water for use, such as foams or rinses, can be used in areas where no sinks are available.
Category III

5. Handwashing Facilities

a. Handwashing facilities should be conveniently located throughout the hospital. *Category I*

b. A sink should be located in or just outside every patient room. More than one sink per room may be necessary if a large room is used for several patients. *Category II*

c. Handwashing facilities should be located in or adjacent to rooms where diagnostic or invasive procedures that require handwashing are performed (e.g., cardiac catheterization, bronchoscopy, sigmoidoscopy, etc.). *Category I*

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Section 2: Cleaning, Disinfecting, and Sterilizing Patient-Care Equipment

INTRODUCTION

Cleaning, the physical removal of organic material or soil from objects, is usually done by using water with or without detergents. Generally, cleaning is designed to remove rather than to kill microorganisms. Sterilization, on the other hand, is the destruction of all forms of microbial life; it is carried out in the hospital with steam under pressure, liquid or gaseous chemicals, or dry heat. Disinfection, defined as the intermediate measures between physical cleaning and sterilization, is carried out with pasteurization or chemical germicides.

Chemical germicides can be classified by several systems. We have used the system originally proposed by Spaulding *(1)* in which three levels of disinfection are defined: high, intermediate, and low (Table 1). In contrast, EPA uses a system that classifies chemical germicides as sporicides, general disinfectants, hospital disinfectants, sanitizers, and others. Formulations registered by the EPA as sporicides are considered sterilants if the contact time is long enough to destroy all forms of microbial life, or high-level disinfectants if contact times are shorter. Chemical germicides registered by the EPA as sanitizers probably fall into the category of low-level disinfectants. Numerous formulations of chemical germicides can be classified as either low- or intermediate-level disinfectants, depending on the specific label claims. For example, some chemical germicide formulations are claimed to be efficacious against *Mycobacterium tuberculosis;* by Spaulding's system, these formulations would be classified at least as intermediate-level disinfectants. However, chemical germicide formulations with specific label claims for effectiveness against *Salmonella cholerea-suis, Staphylococcus aureus*, and *Pseudomonas aeruginosa* (the challenge microorganisms required for EPA classification as a "hospital disinfectant") could fall into intermediate- or low-level disinfectant categories.

The rationale for cleaning, disinfecting, or sterilizing patient-care equipment can be understood more readily if medical devices, equipment, and surgical materials are divided into three general categories (critical items, semicritical items, and noncritical items) based on the potential risk of infection involved in their use. This categorization of medical devices also is based on the original suggestions by Spaulding *(1)*.

Critical items are instruments or objects that are introduced directly into the bloodstream or into other normally sterile areas of the body. Examples of critical items are surgical instruments, cardiac catheters, implants, pertinent components of the heart-lung oxygenator, and the blood compartment of a hemodialyzer. Sterility at the time of use is required for these items; consequently, one of several accepted sterilization procedures is generally recommended.

Items in the second category are classified as semicritical in terms of the degree of risk of infection. Examples are noninvasive flexible and rigid fiberoptic endoscopes, endotracheal tubes, anesthesia breathing circuits, and cystoscopes. Although these items come in contact with intact mucous membranes, they do not ordinarily penetrate body surfaces. If steam sterilization can be used, it is often cheaper to sterilize many of these items, but sterilization is not absolutely essential; at a minimum, a high-level disinfection procedure that can be expected to destroy vegetative microorganisms, most fungal spores, tubercle bacilli, and small nonlipid viruses is recommended. In most cases, meticulous physical cleaning followed by an appropriate high-level disinfection treatment gives the user a reasonable degree of assurance that the items are free of pathogens.

Noncritical items are those that either do not ordinarily touch the patient or touch only intact skin. Such items include crutches, bedboards, blood pressure cuffs, and a variety of other medical accessories. These items rarely, if ever, transmit disease. Consequently, depending on the particular piece of equipment or item, washing with a detergent may be sufficient.

The level of disinfection achieved depends on several factors, principally contact time, temperature, type and concentration of the active ingredients of the chemical germicide, and the nature of the microbial contamination. Some disinfection procedures are capable of producing sterility if the contact times used are sufficiently long; when these procedures are continued long enough to kill all but resistant bacterial spores, the result is high-level disinfection. Other disinfection procedures that can kill many types of viruses and most vegetative microorganisms (but cannot be relied upon to kill resistant microorganisms such as tubercle bacilli, bacterial spores, or certain viruses) are considered to be intermediate- or low-level disinfection (Table 1).

The tubercle bacillus, lipid and nonlipid viruses, and other groups of microorganisms in Table 1 are used in the context of indicator microorganisms that have varying degrees of resistance to chemical germicides and not necessarily because of their importance in causing nosocomial infections. For example, cells of *M. tuberculosis* or *M. bovis*, which are used in routine efficacy tests, are among the most resistant vegetative microorganisms known and, after bacterial endospores, constitute the most severe challenge to a chemical germicide. Thus, a tuberculocidal chemical germicide may be used as a high or intermediate-level disinfectant targeted to many types of nosocomial pathogens but not specifically to control respiratory tuberculosis.

CONTROL MEASURES

Since it is neither necessary nor possible to sterilize all patient-care items, hospital policies can identify whether cleaning, disinfecting, or sterilizing of an item is indicated to decrease the risk of infection. The process indicated for an item will depend on its intended use. Any microorganism, including bacterial spores, that come in contact with normally sterile tissue can cause infection. Thus, it is important that all items that will touch normally sterile tissues be sterilized. It is less important that objects touching mucous membranes be sterile. Intact mucous membranes are generally resistant to infection by common bacterial spores but are not resistant to many other microorganisms, such as viruses and tubercle bacilli; therefore, items that touch mucous membranes require a disinfection process that kills all but resistant bacterial spores. In general, intact skin acts as an effective barrier to most microorganisms; thus, items that touch only intact skin need only be clean.

Items must be thoroughly cleaned before processing, because organic material (e.g., blood and proteins) may contain high concentrations of microorganisms. Also, such organic material may inactivate chemical germicides and protect microorganisms from the disinfection or sterilization process. For many noncritical items, such as blood pressure cuffs or crutches, cleaning can consist only of 1) washing with a detergent or a disinfectant-detergent, 2) rinsing, and 3) thorough drying.

Steam sterilization is the most inexpensive and effective method for sterilization. Steam sterilization is unsuitable, however, for processing plastics with low melting points, powders, or anhydrous oils. Items that are to be sterilized but not used immediately need to be wrapped for storage. Sterility can be maintained in storage for various lengths of time, depending on the type of wrapping material, the conditions of storage, and the integrity of the package.

Several methods have been developed to monitor steam sterilization processes. One method is to check the highest temperature that is reached during sterilization and the length of time that this temperature is maintained. In addition, heat- and steam-sensitive chemical indicators can be used on the outside of each pack. These indicators do not reliably document sterility, but they do show that an item has not accidentally bypassed a sterilization process. As an additional precaution, a large pack might have a chemical indicator both on the outside and the inside to verify that steam has penetrated the pack.

Microbiological monitoring of steam sterilizers is recommended at least once a week with commercial preparations of spores of *Bacillus stearothermophilus* (a microorganism having spores that are particularly resistant to moist heat, thus assuring a wide margin of safety). If a sterilizer is working properly and used appropriately, the spores are usually killed. One positive spore test (spores not killed) does not necessarily indicate that items processed in the sterilizer are not sterile, but it does suggest that the sterilizer should be rechecked for proper temperature, length of cycle, loading, and use and that the test be repeated. Spore testing of steam sterilization is just one of several methods for assuring adequate processing of patient-care items (Table 2).

Implantable items, such as orthopedic devices, require special handling before and during sterilization; thus, packs containing implantable objects need to be clearly labeled so they will be appropriately processed. To guarantee a wide margin of safety, it is recommended that each load of such items be tested with a spore test and that the sterilized item not be released for use until the spore test is negative at 48 hours. If it is not possible to process an implantable object with a confirmed 48-hour spore test before use, it is recommended that the unwrapped object receive the equivalent of full-cycle steam sterilization and *not* flash sterilization. Flash sterilization [270°F (132°C) for 3 minutes in a gravity displacement steam sterilizer] is *not* recommended for implantable items because spore tests cannot be used reliably and the margin of safety is lower.

Because ethylene oxide gas sterilization is a more complex and expensive process than steam sterilization, it is usually restricted to objects that might be damaged by heat or excessive moisture. Before sterilization, objects also need to be cleaned thoroughly and wrapped in a material that allows the gas to penetrate. Chemical indicators need to be used with each package to show that it has been exposed to the gas sterilization process. Moreover, it is recommended that gas sterilizers be checked at least once a week with commercial preparations of spores, usually *Bacillus subtilis* var. *niger*. Because ethylene oxide gas is toxic, precautions (e.g., local exhaust ventilation) should be taken to protect personnel *(2)*. All objects processed by gas sterilization also need special aeration according to manufacturer's recommendations before use to remove toxic residues of ethylene oxide.

Powders and anhydrous oils can be sterilized by dry heat. Microbiological monitoring of dry heat sterilizers and following manufacturers' recommendations for their use and maintenance usually provides a wide margin of safety for dry heat sterilization.

Liquid chemicals can be used for sterilization and disinfection when steam, gas, or dry heat sterilization is not indicated or available. With some formulations, high-level disinfection can be accomplished in 10-30 minutes, and sterilization can be achieved if exposure is for significantly longer times. Nevertheless, not all formulations are equally applicable to all items that need to be sterilized or disinfected. No formulation can be considered as an "all purpose" chemical germicide. In each case, more detailed information can be obtained from the EPA, descriptive brochures from the manufacturers, peer-review journal articles, and books. The most appropriate chemical germicide for a particular situation can be selected by responsible personnel in each hospital based on the object to be disinfected, the level of disinfection needed, and the scope of services, physical facilities, and personnel available in the hospital. It is also important that the manufacturer's instructions for use be consulted.

Gloves may be indicated to prevent skin reactions when some chemical disinfectants are used. Items subjected to high-level disinfection with liquid chemicals need to be rinsed in *sterile* water to remove toxic or irritating residues and then thoroughly dried. Subsequently, the objects need to be handled aseptically with sterile gloves and towels and stored in protective wrappers to prevent recontamination.

Hot-water disinfection (pasteurization) is a high-level, nontoxic disinfection process that can be used for certain items, e.g., respiratory therapy breathing circuits.

In recent years, some hospitals have considered reusing medical devices labeled disposable or single use only. In general, the primary, if not the sole, motivation for such reuse is to save money. For example, the disposable hollow-fiber hemodialyzer has been reprocessed and reused on the same patient in hemodialysis centers since the early 1970s. By 1984, 51% of the 1,200 U.S. dialysis centers were using dialyzer reprocessing programs. It has been estimated that this practice saves more than 100 million dollars per year *(3)*. When standard protocols for cleaning and disinfecting hemodialyzers are used, there does not appear to be any significant infection risk to dialysis patients *(4)*. Moreover, the safety and efficacy of dialyzer reuse programs are supported by several major studies *(5-7)*. Few, if any, other medical devices that might be considered candidates for reprocessing have been evaluated in this manner.

Arguments for and against reprocessing and reusing single-use items in the 1980's have been summarized *(4)*. Since there is lack of evidence indicating increased risk of nosocomial infections associated with reusing *all* single-use items, a categorical recommendation against all types of reuse is not considered justifiable. Rather than recommending for or against reprocessing and reuse of all single-use items, it appears more prudent to recommend that hospitals consider the safety and efficacy of the reprocessing procedure of each item or device separately and the likelihood that the device will function as intended after reprocessing. In many instances it may be difficult if not impossible to document that the device can be reprocessed without residual toxicity and still function safely and effectively. Few, if any, manufacturers of disposable or single-use medical devices provide reprocessing information on the product label.

Hydrotherapy pools and immersion tanks present unique disinfection problems in hospitals. It is generally not economically feasible to drain large hydrotherapy pools that contain thousands of gallons of water after each patient use. Typically, these pools are used by a large number of patients and are drained and cleaned every one to two weeks. The water temperature is typically maintained near 37°C. Between cleanings, water can be contaminated by organic material from patients, and high levels of microbial contamination are possible. One method to maintain safe pool water is to install a water filter of sufficient size to filter all the water at least three times per day and to chlorinate the water so that a *free* chlorine residual of approximately 0.5 mg/l is maintained at a pH of 7.2 to 7.6. Local public health authorities can provide consultation regarding chlorination, alternate halogen disinfectants, and hydrotherapy pool sanitation.

Hubbard and immersion tanks present entirely different problems than large pools, since they are drained after each patient use. All inside surfaces need to be cleaned with a disinfectant-detergent, then rinsed with tap water. After the last patient each day, an additional disinfection step is performed. One general procedure is to circulate a chlorine solution (200-300 mg/l) through the agitator of the tank for 15 minutes and then rinse it out. It is also recommended that the tank be thoroughly cleaned with a disinfectant-detergent, rinsed, wiped dry with clean cloths, and not filled until ready for use.

An alternative approach to control of contamination in hydrotherapy tanks is to use plastic liners and create the "whirlpool effect" without agitators. Such liners make it possible to minimize contact of contaminated water with the interior surface of the tank and also obviate the need for agitators that may be very difficult to clean and decontaminate.

RECOMMENDATIONS

1. **Cleaning**
   All objects to be disinfected or sterilized should first be thoroughly cleaned to remove all organic matter (blood and tissue) and other residue. *Category I*
2. **Indications for Sterilization and High-Level Disinfection**
   a. Critical medical devices or patient-care equipment that enter normally sterile tissue or the vascular system or through which blood flows should be subjected to a sterilization procedure before each use. *Category I*
   b. Laparoscopes, arthroscopes, and other scopes that enter normally sterile tissue should be subjected to a sterilization procedure before each use; if this is not feasible, they should receive at least high-level disinfection. *Category I*
   c. Equipment that touches mucous membranes, e.g., endoscopes, endotracheal tubes, anesthesia breathing circuits, and respiratory therapy equipment, should receive high-level disinfection. *Category I*
3. **Methods of Sterilization**
   a. Whenever sterilization is indicated, a steam sterilizer should be used unless the object to be sterilized will be damaged by heat, pressure, or moisture or is otherwise inappropriate for steam sterilization. In this case, another acceptable method of sterilization should be used. *Category II*
   b. Flash sterilization [270°F (132°C) for 3 minutes in a gravity displacement steam sterilizer] is not recommended for implantable items. *Category II*
4. **Biological Monitoring of Sterilizers**
   a. All sterilizers should be monitored at least once a week with commercial preparations of spores intended specifically for that type of sterilizer (i.e., *Bacillus stearothermophilus* for steam sterilizers and *Bacillus subtilis* for ethylene oxide and dry heat sterilizers). *Category II*
   b. Every load that contains implantable objects should be monitored. These implantable objects should not be used until the spore test is found to be negative at 48 hours. *Category II*
   c. If spores are not killed in *routine* spore tests, the sterilizer should immediately be checked for proper use and function and the spore test repeated. Objects, other than implantable objects, do not need to be recalled because of a single positive spore test unless the sterilizer or the sterilization procedure is defective. *Category II*
   d. If spore tests remain positive, use of the sterilizer should be discontinued until it is serviced. *Category I*
5. **Use and Preventive Maintenance**
   Manufacturers' instructions should be followed for use and maintenance of sterilizers. *Category II*

6. Chemical Indicators

Chemical indicators that will show a package has been through a sterilization cycle should be visible on the outside of each package sterilized. *Category II*

7. Use of Sterile Items

An item should not be used if its sterility is questionable, e.g., its package is punctured, torn, or wet. *Category I*

8. Reprocessing Single-Use or Disposable Items

a. Items or devices that cannot be cleaned and sterilized or disinfected without altering their physical integrity and function should not be reprocessed. *Category I*

b. Reprocessing procedures that result in residual toxicity or compromise the overall safety or effectiveness of the items or devices should be avoided. *Category I*

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Section 3: Microbiologic Sampling

INTRODUCTION

Before 1970, regularly scheduled culturing of the air and environmental surfaces such as floors, walls, and table tops was widely practiced in U.S. hospitals. By 1970, CDC and the American Hospital Association were advocating that hospitals discontinue routine environmental culturing, since rates of nosocomial infection had not been related to levels of general microbial contamination of air or environmental surfaces, and meaningful standards for permissible levels of microbial contamination of environmental surfaces did not exist *(1,2)*. Between 1970 and 1975, 25% of U.S. hospitals reduced the extent of such routine environmental culturing *(3)*, and this trend has continued.

In the last several years, there has also been a trend toward reducing routine microbiologic sampling for quality control purposes. In 1982, CDC recommended that the disinfection process for respiratory therapy equipment should not be monitored by routine microbiologic sampling *(4)*. Moreover, the recommendation for microbiologic sampling of infant formulas prepared in the hospital has been removed from this *Guideline*, since there is no epidemiologic evidence to show that such quality control testing influences the infection rate in hospitals.

CONTROL MEASURES

The only routine or periodic microbiologic sampling that is recommended is of the water and dialysis fluids used with artificial kidney machines in hospital-based or free standing chronic hemodialysis centers. Microbiologic sampling of dialysis fluids and water used to prepare dialysis fluids is recommended because gram-negative bacteria are able to grow rapidly in water and other fluids associated with the hemodialysis system; high levels of these microorganisms place dialysis patients at risk of pyrogenic reactions, bacteremia, or both *(5)*. It is suggested that the water that is used to prepare dialysis fluid also be sampled periodically, because high levels of bacteria in water often become amplified downstream in a hemodialysis system and are sometimes predictive of bacterial contamination in dialysis fluids. Although it is difficult to determine the exact frequency of such a sampling program in the absence of pyrogenic reactions and bacteremia, sampling water and dialysis fluid monthly appears to be reasonable.

Routine microbiologic sampling of patient-care items purchased as sterile is not recommended because of the difficulty and expense of performing adequate sterility testing with low-frequency contamination.

Microbiologic sampling is indicated during investigation of infection problems if environmental reservoirs are implicated epidemiologically in disease transmission. It is important, however, that such culturing be based on epidemiologic data and follow a written plan that specifies the objects to be sampled and the actions to be taken based on culture results.

RECOMMENDATIONS

1. **Routine Environmental Culturing of Air and Environmental Surfaces**
   Routine microbiologic sampling of the air and environmental surfaces should not be done. *Category I*
2. **Microbiologic Sampling of Dialysis Fluids**
   Water used to prepare dialysis fluid should be sampled once a month; it should not contain a total viable microbial count greater than 200 colony-forming units (CFU)/ml. The dialysis fluid should be sampled once a month at the end of a dialysis treatment and should contain less than 2,000 CFU/ml. *Category II*
3. **Microbiologic Sampling for Specific Problems**
   Microbiologic sampling, when indicated, should be an integral part of an epidemiologic investigation. *Category I*
4. **Sampling for Manufacturer-Associated Contamination**
   a. Routine microbiologic sampling of patient-care objects purchased as sterile is not recommended. *Category I*
   b. If contamination of a commercial product sold as sterile is suspected, infection control personnel should be notified, suspect lot numbers should be recorded, and items from suspected lots should be segregated and quarantined. Appropriate microbiologic assays may be considered; however, the nearest district office of the FDA, local and state health departments, and CDC should be notified promptly. *Category I*

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Section 4: Infective Waste

INTRODUCTION

There is no epidemiologic evidence to suggest that most hospital waste is any more infective than residential waste. Moreover, there is no epidemiologic evidence that hospital waste disposal practices have caused disease in the community. Therefore, identifying wastes for which special precautions are indicated is largely a matter of judgment about the relative risk of disease transmission. Aesthetic and emotional considerations may override the actual risk of disease transmission, particularly for pathology wastes.

Since a precise definition of infective waste that is based on the quantity and type of etiologic agents present is virtually impossible, the most practical approach to infective waste management is to identify those wastes that represent a sufficient potential risk of causing infection during handling and disposal and for which some special precautions appear prudent. Hospital wastes for which special precautions appear prudent include microbiology laboratory waste, pathology waste, and blood specimens or blood products. Moreover, the risk of either injury or infection from certain sharp items (e.g., needles and scalpel blades) contaminated with blood also needs to be considered when such items are disposed of. While any item that has had contact with blood, exudates, or secretions may be potentially infective, it is not normally considered practical or necessary to treat all such waste as infective. CDC has published general recommendations for handling infective waste from patients on isolation precautions *(1)*. Additional special precautions may be necessary for certain rare diseases or conditions such as Lassa fever *(2)*. The EPA has published a draft manual (Environmental Protection Agency. Office of Solid Waste and Emergency Response. Draft Manual for Infectious Waste Management, SW-957, 1982. Washington: 1982) that identifies and categorizes other specific types of waste that may be generated in some research-oriented hospitals. In addition to the above guidelines, local and state environmental regulations may also exist.

CONTROL MEASURES

Solid waste from the microbiology laboratory can be placed in steam-sterilizable bags or pans and steam-sterilized in the laboratory. Alternatively, it can be transported in sealed, impervious plastic bags to be burned in a hospital incinerator. A single bag is probably adequate if the bag is sturdy (not easily penetrated) and if the waste can be put in the bag without contaminating the outside of the bag; otherwise, double-bagging is indicated. All slides or tubes with small amounts of blood can be packed in sealed, impervious containers and sent for incineration or steam sterilization in the hospital. Exposure for up to 90 minutes at 250°F (121°C) in a steam sterilizer, depending on the size of the load and type container, may be necessary to assure an adequate sterilization cycle *(3,4)*. After steam sterilization, the residue can be safely handled and discarded with all other nonhazardous hospital solid waste. All containers with more than a few milliliters of blood remaining after laboratory procedures and/or bulk blood may be steam sterilized, or the contents may be carefully poured down a utility sink drain or toilet.

Waste from the pathology laboratory is customarily incinerated at the hospital. Although no national data are available, in one state 96% of the hospitals surveyed reported that they incinerate pathology waste *(5)*. Any hospital incinerator should be capable of burning, within applicable air pollution regulations, the actual waste materials to be destroyed. Improper incineration of waste with high moisture and low energy content, such as pathology waste, can lead to emission problems.

Disposables that can cause injury, such as scalpel blades and syringes with needles, should be placed in puncture-resistant containers. Ideally, such containers are located where these items are used. Syringes and needles can be placed intact directly into the rigid containers for safe storage until terminal treatment. To prevent needle-stick injuries, needles should not be recapped, purposely bent, or broken by hand. When some needle-cutting devices are used, blood may be aerosolized or spattered onto environmental surfaces; however, currently no data are available from controlled studies examining the effect, if any, of the use of these devices on the incidence of needle-transmissible infections.

It is often necessary to transport or store infective waste within the hospital prior to terminal treatment. This can be done safely if proper and common-sense procedures are used. The EPA draft manual mentioned above contains guidelines for the storage and transport, both on-site and off-site, of infective waste. For unique and specialized problems, this manual can be consulted.

RECOMMENDATIONS

1. Identification of Infective Waste

a. Microbiology laboratory wastes, blood and blood products, pathology waste, and sharp items (especially needles) should be considered as potentially infective and handled and disposed of with special precautions. *Category II*

b. Infective waste from patients on isolation precautions should be handled and disposed of according to the current edition of the *Guideline for Isolation Precautions in Hospitals*. (This recommendation is not categorized since the recommendations for isolation precautions are not categorized.)

2. Handling, Transport, and Storage of Infective Waste

a. Personnel involved in the handling and disposal of infective waste should be informed of the potential health and safety hazards and trained in the appropriate handling and disposal methods.
Category II

b. If processing and/or disposal facilities are not available at the site of infective waste generation (i.e., laboratory, etc.) the waste may be safely transported in sealed impervious containers to another hospital area for appropriate treatment. *Category II*

c. To minimize the potential risk for accidental transmission of disease or injury, infective waste awaiting terminal processing should be stored in an area accessible only to personnel involved in the disposal process. *Category III*

3. Processing and Disposal of Infective Waste

a. Infective waste, in general, should either be incinerated or should be autoclaved prior to disposal in a sanitary landfill. *Category III*

b. Disposable syringes with needles, scalpel blades, and other sharp items capable of causing injury should be placed intact into puncture-resistant containers located as close to the area in which they were used as is practical. To prevent needle-stick injuries, needles should not be recapped, purposely bent, broken, or otherwise manipulated by hand. *Category I*

c. Bulk blood, suctioned fluids, excretions, and secretions may be carefully poured down a drain connected to a sanitary sewer. Sanitary sewers may also be used for the disposal of other infectious wastes capable of being ground and flushed into the sewer. *Category II* (Special precautions may be necessary for certain rare diseases or conditions such as Lassa fever *(2)*.)

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Section 5: Housekeeping

INTRODUCTION

Although microorganisms are a normal contaminant of walls, floors, and other surfaces, these environmental surfaces rarely are associated with transmission of infections to patients or personnel. Therefore, extraordinary attempts to disinfect or sterilize these environmental surfaces are rarely indicated. However, routine cleaning and removal of soil are recommended. Recommendations for cleaning in the rooms of patients on isolation precautions have been published *(1)*.

CONTROL MEASURES

Cleaning schedules and methods vary according to the area of the hospital, type of surface to be cleaned, and the amount and type of soil present. Horizontal surfaces (for example, bedside tables and hard-surfaced flooring) in patient-care areas are usually cleaned on a regular basis, when soiling or spills occur, and when a patient is discharged. Cleaning of walls, blinds, and curtains is recommended only if they are visibly soiled. Disinfectant fogging is an unsatisfactory method of decontaminating air and surfaces and is not recommended.

Recommendations against use of carpets in patient-care areas have been removed from this *Guideline*, since there is no epidemiologic evidence to show that carpets influence the nosocomial infection rate in hospitals *(2)*. Carpets, however, may contain much higher levels of microbial contamination than hard-surfaced flooring and can be difficult to keep clean in areas of heavy soiling or spillage; therefore, appropriate cleaning and maintenance procedures are indicated.

Disinfectant-detergent formulations registered by the EPA can be used for environmental surface cleaning, but the actual physical removal of microorganisms by scrubbing is probably as important, if not more so, than any antimicrobial effect of the cleaning agent used. Therefore, cost, safety, and acceptability by housekeepers can be the main criteria for selecting any such registered agent. The manufacturers' instructions for appropriate use should be followed.

Special precautions for cleaning incubators, mattresses, and other nursery surfaces with which neonates have contact have been recommended *(3)*, since inadequately diluted solutions of phenolics used for such cleaning and poor ventilation have been associated with hyperbilirubinemia in newborns *(4)*.

RECOMMENDATIONS

1. Choice of Cleaning Agent for Environmental Surfaces in Patient-Care Areas

Any hospital-grade disinfectant-detergent registered by the EPA may be used for cleaning environmental surfaces. Manufacturers' instructions for use of such products should be followed. *Category II*

2. Cleaning of Horizontal Surfaces in Patient-care Areas

a. Uncarpeted floors and other horizontal surfaces, e.g., bedside tables, should be cleaned regularly and if spills occur. *Category II*

b. Carpeting should be vacuumed regularly with units designed to efficiently filter discharged air, cleaned if spills occur, and shampooed whenever a thorough cleaning is indicated. *Category II*

3. Cleaning Walls, Blinds, and Curtains

Terminal cleaning of walls, blinds, and curtains is not recommended unless they are visibly soiled. *Category II*

4. Disinfectant fogging

Disinfectant fogging should not be done. *Category I*

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Section 6: Laundry

INTRODUCTION

Although soiled linen has been identified as a source of large numbers of pathogenic microorganisms, the risk of actual disease transmission appears negligible. Rather than rigid rules and regulations, hygienic and common-sense storage and processing of clean and soiled linen are recommended. Guidelines for laundry construction and operation for health care facilities have been published *(1,2)*.

CONTROL MEASURES

Soiled linen can be transported in the hospital by cart or chute. Bagging linen is indicated if chutes are used, since improperly designed chutes can be a means of spreading microorganisms throughout the hospital *(3)*. Recommendations for handling soiled linen from patients on isolation precautions have been published *(4)*.

Soiled linen may or may not be sorted in the laundry before being loaded into washer/extractor units. Sorting before washing protects both machinery and linen from the effects of objects in the linen and reduces the potential for recontamination of clean linen that sorting after washing requires. Sorting after washing minimizes the direct exposure of laundry personnel to infective material in the soiled linen and reduces airborne microbial contamination in the laundry *(5)*. Protective apparel and appropriate ventilation *(2)* can minimize these exposures.

The microbicidal action of the normal laundering process is affected by several physical and chemical factors *(5)*. Although dilution is not a microbicidal mechanism, it is responsible for the removal of significant quantities of microorganisms. Soaps or detergents loosen soil and also have some microbicidal properties. Hot water provides an effective means of destroying microorganisms, and a temperature of at least 71°C (160°F) for a minimum of 25 minutes is commonly recommended for hot-water washing. Chlorine bleach provides an extra margin of safety. A total available chlorine residual of 50-150ppm is usually achieved during the bleach cycle. The last action performed during the washing process is the addition of a mild acid to neutralize any alkalinity in the water supply, soap, or detergent. The rapid shift in pH from approximately 12 to 5 also may tend to inactivate some microorganisms.

Recent studies have shown that a satisfactory reduction of microbial contamination can be achieved at lower water temperatures of 22-50°C when the cycling of the washer, the wash formula, and the amount of chlorine bleach are carefully monitored and controlled *(6,7)*. Instead of the microbicidal action of hot water, low-temperature laundry cycles rely heavily on the presence of bleach to reduce levels of microbial contamination. Regardless of whether hot or cold water is used for washing, the temperatures reached in drying and especially during ironing provide additional significant microbicidal action.

RECOMMENDATIONS

1. Routine Handling of Soiled Linen

- a. Soiled linen should be handled as little as possible and with minimum agitation to prevent gross microbial contamination of the air and of persons handling the linen. *Category II*
- b. 1) All soiled linen should be bagged or put into carts at the location where it was used; it should *not* be sorted or prerinsed in patient-care areas. *Category II*
  - 2) Linen soiled with blood or body fluids should be deposited and transported in bags that prevent leakage. *Category II*
- c. If laundry chutes are used, linen should be bagged, and chutes should be properly designed. *Category II*

2. Hot-Water Washing

If hot water is used, linen should be washed with a detergent in water at least 71°C (160°F) for 25 minutes. *Category II*

3. Low-Temperature Water Washing

If low temperature (< 70°C) laundry cycles are used, chemicals suitable for low-temperature washing at proper use concentration should be used. *Category II*

4. Transportation of Clean Linen

Clean linen should be transported and stored by methods that will ensure its cleanliness. *Category II*

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Table 1. Levels of Disinfection According to Type of Microorganism

	Bacteria			Fungi[1]	Viruses	
Levels	**Vegetative**	**Tubercle Bacillus**	**Spores**		**Lipid & Medium size**	**Nonlipid & Small**
High	+[2]	+	+[3]	+	+	+
Intermediate	+	+	±[4]	+	+	±[5]
Low	+	–	–	±	+	–

[1] Includes asexual spores but not necessarily chlamydospores or sexual spores

[2] Plus sign indicates that a killing effect can be expected when the normal use-concentrations of chemical disinfectants or pasteurization are properly employed; a negative sign indicates little or no killing effect

[3] Only with extended exposure times are high-level disinfectant chemicals capable of actual sterilization

[4] Some intermediate-level disinfectants can be expected to exhibit some sporicidal action

[5] Some intermediate-level disinfectants may have limited virucidal activity

Table 2. Methods of Assuring Adequate Processing and Safe Use of Medical Devices

Object and Classification	Example	Method	Comment
PATIENT-CARE OBJECTS			
Critical			
Sterilized in the hospital	Surgical instruments and devices; trays and sets	1. Thoroughly clean objects and wrap or package for sterilization. 2. Follow manufacturer's instructions for use of each sterilizer or use recommended protocol. 3. Monitor time-temperature charts. 4. Use commercial spore preparations to monitor sterilizers. 5. Inspect package for integrity and for exposure of sterility indicator before use. 6. Use before maximum safe storage time has expired if applicable.	Sterilization processes are designed to have a wide margin of safety. If spores are not killed, the sterilizer should be checked for proper use and function; if spore tests remain positive, discontinue use of the sterilizer until properly serviced. Maximum safe storage time of items processed in the hospital varies according to type of package or wrapping material(s) used; follow manufacturer's instructions for use and storage times.
Purchased as sterile	Intravenous fluids; irrigation fluids; normal saline; trays and sets	1. Store in safe, clean area. 2. Inspect package for integrity before use. 3. Use before expiration date if one is given. 4. Culture only if clinical circumstances suggest infection related to use of the item.	Notify the Food and Drug Administration, local and state health departments, and CDC if intrinsic contamination is suspected.
Semicritical			
Should be free of vegetative bacteria. May be subjected to high-level disinfection rather than sterilization process	Respiratory therapy equipment and instruments that will touch mucous membranes	1. Sterilize or follow a protocol for high-level disinfection. 2. Bag and store in safe, clean area. 3. Conduct quality control monitoring after any important changes in the disinfection process.	Bacterial spores may survive after high-level disinfection, but these usually are not pathogenic. Microbiologic sampling can verify that a high-level disinfection process has resulted in destruction of vegetative bacteria; however, this sampling is not routinely recommended.
Non critical			
Usually contaminated with some bacteria	Bedpans; crutches; rails; EKG leads	1. Follow a protocol for cleaning or, if necessary a low-level disinfection process.	
Water-produced or treated	Water used for hemodialysis fluids	1. Assay water and dialysis fluids monthly. 2. Water should not have more than 200 bacteria/ml and dialysis fluids not more than 2000 bacteria/ml.	Gram-negative water bacteria can grow rapidly in water and dialysis fluids and can place dialysis patients at risk of pyrogenic reactions or septicemia. These water sources and pathways should be disinfected routinely.

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Senator **Sarbanes**. Thank you, Dr. Rheinstein.

First, for the record, gentlemen, would you outline the responsibilities of the office you hold, and give us also, for the record, a review of your own career record and of your qualifications for the job you're now doing. I think in a courtroom they call this qualifying the expert witness.

Dr. Rheinstein, why don't you do that first and then we'll turn to Mr. Campt.

Dr. **Rheinstein**. I'm Director of the Office of Drug Standards within the Center for Drugs and Biologics. The Office of Drug Standards is composed of five operating divisions comprising in the aggregate about 170 or 180 people.

These five divisions are the Division of Over-the-Counter Drug Products with which we're primarily concerned today; the Division of Drug Advertising and Labeling which regulates promotion of prescription drug products; the Division of Generic Drugs which approves applications for drug products which are copies of other products already in the marketplace; the Division of Biopharmaceutics which traces the absorption, distribution, metabolism, and elimination of drug products within the body; and finally, the Division of Bioequivalence which assures that different brands of the same products—in other words, brand name drugs and generic drugs—reach the same blood level and, hence, have the same therapeutic effects.

My qualifications—I have a bachelor of arts with high honors and a master of science in mathematics from Michigan State University in East Lansing, Michigan. I have my doctor of medicine from Johns Hopkins University in Baltimore, Maryland; and I have a law degree from the University of Maryland School of Law, also in Baltimore.

I am licensed to practice medicine in Maryland, California, New York, and the District of Columbia and admitted to the bar in Maryland and in the District of Columbia.

I came to the Food and Drug Administration in 1974 from a position in the Department of Medicine at the University of Maryland. I had assumed that position after completing my time in the U.S. Public Health Service. I am board certified in family practice and was recertified most recently in 1983.

I have an interest in a number of outside organizations which are involved in programs to educate professionals and the public regarding drugs, drug development, and drug regulation. These include the Federal Bar Association, where I was chairman of the Food and Drug Committee from 1976 to 1979; the Drug Information Association, of which I was president last year and of which I am currently vice president; and the American College of Legal Medicine which is the professional society for physician-attorneys, and of that group I am currently the treasurer.

Senator **Sarbanes**. You've been with the FDA since 1974?

Dr. **Rheinstein**. Yes.

Senator **Sarbanes**. Within the Office of Drug Standards throughout that period of time?

Dr. **Rheinstein**. Well, FDA has had a number of reorganizations. So prior to 2 or 3 years ago there was no Office of Drug Standards. I began as Director of what was then called the Division of Drug

Advertising in 1974. That division regulated promotion of prescription drug products.

In 1981, the drug labeling staff was merged into that division and I remained as Director of the combined division, so we looked also at the labeling of prescription drug products.

In 1982, we had a major reorganization within the agency. The Center for Drugs and Biologics was formed out of what had been the Bureau of Drugs and a separate Bureau of Biologics. At that time, the Center for Drugs and Biologics was divided into three principal offices, of which I was initially a deputy director and later director of the Office of Drugs, which included all of what is now the Office of Drug Standards plus some other functions.

We then had another reorganization in 1983 and I became Director of the Office of Drug Standards.

Senator Sarbanes. Mr. Campt, if you could briefly give us a similar review.

Mr. Campt. Yes, sir. I am currently Director of the Office of Pesticide Programs in the Office of Pesticides and Toxic Substances. That Office has about 600 people in five divisions involving a Hazard Evaluation Division, a Registration Division, a Benefits and Use Division, and a Program Management and Support Division.

The program is responsible for regulating pesticides, including insecticides, fungicides, herbicides, and disinfectants. It is responsible for premarket clearance and registration of products of that type prior to being used in the United States.

I have been with EPA since its inception in 1970. Prior to that time, I was with the U.S. Department of Agriculture when the responsibility for regulating pesticides was in that organization. I joined the Pesticide Regulation Division of the U.S. Department of Agriculture in 1966. Prior to that time, I was a plant quarantine inspector at John F. Kennedy International Airport in New York with the U.S. Department of Agriculture.

I have held a number of positions in both the U.S. Department of Agriculture involved in the regulation of pesticides since 1966.

I have a bachelor of science degree in biology from North Carolina Central University in Durham, North Carolina. I have done graduate study at Howard University.

Senator Sarbanes. I'm sorry. I missed something. How long have you been the Director of the Office of Pesticide Programs?

Mr. Campt. I have been Director of the Office of Pesticide Programs for just over 3 months. Prior to that time, I was Director of the Registration Division in the Office of Pesticide Programs.

Senator Sarbanes. And how long had you been the Director of the Registration Division?

Mr. Campt. For about 6 years.

Senator Sarbanes. All right. We are very pleased to have been joined by Senator Gore, who's had a very keen interest in this subject matter and by Congresswoman Fiedler of California. I wil defer to them in case they want to make a statement at this point.

Senator Gore. Mr. Chairman, thank you very much. With your consent, I will put the full opening statement I had wanted to give at the beginning of this hearing in the record. I was unavoidably detained by an appearance at another subcommittee.

Senator **Sarbanes**. With objection, the full statement will be included.

[The written opening statement of Senator Gore follows:]

WRITTEN OPENING STATEMENT OF HON. ALBERT GORE, JR.

Thank you Mr. Chairman.

I want to commend you for calling a second hearing on hospital disinfectants and antiseptics. Without your leadership we would not have had these two opportunities to explore the threat to thousands of patients in hospitals across the country.

In the hearing on August 7, we heard disturbing testimony about the woefully inadequate regulation of antiseptics, many of which contain the same active ingredients as disinfectants. Dr. William Rutala observed that "there is no standardized protocol required by the FDA for efficacy testing of antiseptics."

That testimony raises several serious questions. Just how is the effectiveness of hospital antiseptics determined? Do we simply take the manufacturer's word for it? Does the FDA do anything to monitor antiseptic effectiveness in the market place?

Documents released at the last hearing showed us that 20 percent of all disinfectants regulated by EPA were ineffective. Now we learn there are no FDA standards for effectiveness testing of antiseptics.

Apparently there is nothing to stop some company from going into business as "Antiseptics-R-Us" and producing antiseptics without ever having to prove that they work in the market place.

How many of the two million infections acquired in hospitals each year are the result of ineffective antiseptics?

Far too many, judging from a review of the literature.

o In 1984 an article in the APPLIED AND ENVIRONMENTAL MICROBIOLOGY magazine described bacterial contamination of an iodophor solution used in preoperative skin preparation.

Five patients became infected from this faulty antiseptic.

o In 1982 several patients became infected from contaminated chlorhexidine antiseptic solutions used in postoperative wounds, according to an article in the JOURNAL OF HOSPITAL INFECTION.

o There have been so many outbreaks of nosocomial infections associated with quaternary ammonium products, commonly used to clean skin wounds, that the Centers for Disease Control has recommended against their use as antiseptics.

What has FDA done to protect the American people from these ineffective or contaminated products?

I look forward to hearing the FDA witness answer that question. I also am interested in hearing the views of our witness from EPA on the disinfectant amendment to FIFRA recently passed in the House.

Mr. Chairman, since the August 7th hearing, several Members of the House, including Mr. Scheuer, introduced legislation identical to the bill I introduced in the Senate, to require the monitoring of disinfectants. Last Friday that provision was attached to the FIFRA amendments, and passed the House unanimously with the blessing of industry, academia and EPA.

I have been gratified by the overwhelming support for improved monitoring of disinfectants. I hope this hearing will give us the information we need to strengthen our efforts to improve the effectiveness of antiseptics. The American people count on antiseptics and disinfectants to protect them from infection. It is our job to see that they work.

Senator GORE. I appreciate that. Let me just say a few brief words.

First of all, Mr. Chairman, I want to thank you for your active interest and support in this area. Since we joined efforts in the August 7 hearing on disinfectants primarily, legislation identical to the bill that I introduced here in the Senate to require the monitoring of disinfectants has passed in the House of Representatives. One member of the House who joined in the last hearing introduced that legislation after the hearing and last Friday that provision was attached to the FIFRA amendments and passed the House unanimously, and I'm very pleased by that.

I hope that we can do the same thing either today or tomorrow when the FIFRA bill comes here.

Today, we turn to the related subject of antiseptics. Our concern was focused on antiseptics really in that first hearing and we talked about it and decided, well, yes, this is an equally important subject that really needs attention. And the more I've studied it, the more I've come to agree with this focus. And I hope that today's hearing will serve to strengthen our efforts to improve the effectiveness of antiseptics.

If you look at this in a broad context, it's absolutely incredible that we have 2 million hospital-caused infections every single year; and 20,000 of them result in deaths each year.

Now what do hospitals do in order to combat this extremely serious problem, this great tragedy, and a very expensive matter I might add?

Well, they turn first of all as their first line of defense to disinfectants and antiseptics. But today, there is apparently absolutely nothing to stop a company from going into business as "Antiseptics Are Us," and selling into the market antiseptics that have never been proven to work at all.

Now the Food and Drug Administration recognized this problem some time ago and there was a tentative final rule published back in 1978. But since that time, the FDA has been dragging its feet and doing absolutely nothing on this matter and, still, this final rule is pending and has not been promulgated. They don't even take the step of making a company accountable for the statements they make on their labels. They can put inaccurate labels on antiseptics with instructions that are completely contrary to what the scientific evidence shows are necessary to use the antiseptics properly.

In 1984, an article in the Applied and Environmental Microbiology magazine described bacterial contamination in an iodophor solution used in preoperative skin preparation. Five patients became infected from this faulty antiseptic.

In 1982 several patients became infected from contaminated chlorhexidine antiseptic solutions used in postoperative wounds, according to an article in the Journal of Hospital Infection.

There have been so many outbreaks of nosocomial infections associated with quaternary ammonium products, commonly used to clear skin wounds, that the Centers for Disease Control have recommended against their use as antiseptics.

As we get into the questions I will get into some examples of these products that don't work, that are mislabeled, and ask some questions about why the Food and Drug Administration refuses to do anything about it.

So, Mr. Chairman, I'm pleased that we've made such rapid progress on the disinfectant part of this problem. I hope we can now repeat that progress in the antiseptic area and I look forward to questioning the witnesses after you.

Senator SARBANES. Fine.

Gentlemen, let me ask you, did you obtain copies of the statements given to the committee at the August 7 hearing, and review them in preparation for this hearing?

Mr. CAMPT. Mr. Chairman, I have not reviewed them recently. I think I saw them early in the process.

Senator SARBANES. You mean back about the time they were given before the subcommittee?

Mr. CAMPT. That's correct.

Senator SARBANES. Dr. Rheinstein.

Dr. RHEINSTEIN. We did not obtain them until fairly recently. We asked for them after we received the letter of invitation to today's hearing. So we received them—at least my office received them about 2 or 3 days ago.

Senator SARBANES. I have to say to both of you in all candor that I am struck by the gap between the problem as it has been defined to the subcommittee in terms of nosocomial infections, both from disinfectants and antiseptics, in the testimony we received about 6 weeks ago, which emphasized the need to address the problem, and the level of response this morning in these two statements, which in effect suggest there's really not much of a problem. You seem to be saying there's not really much we need to do, things are really going along more or less all right, although we recognize some deficiencies.

I have to say I am struck by what I perceive to be an enormous gap between some very recent expert testimony about the problem and how to respond to it, and the nature of the response that's embraced in your two statements this morning.

Just to get this on the record, Mr. Campt, let me ask you, when a manufacturer registers a disinfectant with the EPA, does that registration represent EPA's assurance to the consumer that the disinfectant is safe and effective when used as directed?

Mr. CAMPT. I think the statutory standard is that the product can be used as directed without causing unreasonable adverse effect on the environment.

The only question I would have with your characterization would be the term "safe" in terms of absolute safety. I think that we have a risk-benefit statute where we need to balance the risks from using the pesticide against the benefits—the risk-benefit balancing—and I would only state it is not an absolute safety standard.

Senator SARBANES. Well, I'm not sure of the answer to my questions. When you register the disinfectant at the EPA, what are you representing to the consumer? Are you representing to the consumer that that disinfectant is safe and effective?

Mr. CAMPT. I think we represent that the product will perform its intended function without unreasonable adverse effects on the environment and we base that determination on studies that we require from the applicant through registration that we review and we make that judgment based on those studies.

Senator **Sarbanes**. Who tests to make sure that the disinfectant is safe and effective?

Mr. **Campt**. We rely on studies that—we've published guidelines that indicate the studies that are needed to support registration. The appliant for registration is required to produce those studies in his application for registration, along with all claims that are to be made for the product.

Senator **Sarbanes**. So the maker of the product tests the product in order to assert to you that it is safe and effective, is that correct?

Mr. **Campt**. That is correct.

Senator **Sarbanes**. What procedure does EPA use to assure that the manufacturer actually performs the required efficacy tests and that the data are accurate?

Mr. **Campt**. Well, we would review the data based on the protocols that we have laid out and if we have questions as to whether the data were conducted in accordance with the protocols we've outlined we have procedures for auditing studies, but generally——

Senator **Sarbanes**. What do you mean, you review the data? You look at it to see if it's internally consistent?

Mr. **Campt**. Yes. We look at the data, how it was conducted, whether it was conducted in accordance with the protocols that have been accepted. We look at the conclusions in terms of the effectiveness of the product.

Senator **Sarbanes**. Well, how do you determine, first, that the test was actually done and, second, that the data are accurate?

Mr. **Campt**. Well, there are statutes that would require that the applicant not submit to us falsified tests.

Senator **Sarbanes**. I understand that. How do you determine that that has not happened?

Mr. **Campt**. Well, that would be through audit programs that—we have the authority to audit any test that is submitted to us and require the raw data, go to the laboratory.

Senator **Sarbanes**. How often do you audit?

Mr. **Campt**. I would think that that is probably infrequently, at least with respect to efficacy studies.

Senator **Sarbanes**. How infrequently?

Mr. **Campt**. I don't have information with me in terms of how many studies we have audited over a period of time, but I certainly could——

Senator **Sarbanes**. Would you have done hundreds of such audits this year?

Mr. **Campt**. No.

Senator **Sarbanes**. Tens, dozens?

Mr. **Campt**. We would have done dozens of audits with respect to health and safety studies.

Senator **Sarbanes**. No, no. I want to focus exactly and very specifically on what we're talking about now. How many audits have you done to address this question whether the test was actually performed and whether the data submitted were accurate?

Mr. **Campt**. I don't have those figures before me, Senator. We could certainly provide that information to you. But I would estimate that there have been relatively few audits of that nature during the past year.

Senator **Gore**. Would the chairman yield briefly?

Senator **Sarbanes**. Surely.

Senator **Gore**. Have there been any this year?

Mr. **Campt**. I cannot recall that, but I would like to check the record.

Senator **Gore**. I think the record will probably show there have been zero.

Senator **Sarbanes**. Now given that, what assurance, other than the manufacturer's, does the hospital patient have under current EPA procedures that the disinfectants used by the hospital actually work?

Mr. **Campt**. I think generally the reliance is on the fact that the Agency has reviewed the studies that have been submitted by the applicant and has judged that the product could be used effectively. I am not aware of any other assurances that they might have unless the hospital decided to do their own testing.

Senator **Sarbanes**. Well, there are some who have said—and I think this is worth pursuing—they don't see why we don't let the users use the disinfectant. If it doesn't work they say, people will stop using it, and then the manufacturer will no longer be able to sell his disinfectant.

Do you feel that that acts as an effective check? In other words, a manufacturer tries to sell a disinfectant. He puts it on the market. He makes certain claims for it. He gets a registration from the EPA, which I'm increasingly coming to think is relatively pro forma. In any event, if it doesn't work, users will stop using it; then the manufacturer won't be able to sell it, the manufacturers who make effective disinfectants will sell theirs, and the market will sort this problem out.

Now what about that approach?

Mr. **Campt**. Mr. Chairman, I don't think that is a reasonable approach to regulating disinfectants. We have the authority to waive efficacy testing, the statutory authority. The Agency has elected not to waive efficacy testing on disinfectants because the user cannot readily determine whether a hospital disinfectant will work.

With respect to other pesticide products that we regulate, that is, herbicides or insecticides, the user can discern whether or not the product is working by virtue of whether the bugs are killed or the weeds are destroyed.

That is not the case with respect to antimicrobials, including disinfectants, and the Agency's policy is not to waive data on those types of products.

Senator **Sarbanes**. If a hospital suspects that a disinfectant does not work, how does the EPA under its current procedures determine whether or not the disinfectant is effective?

Mr. **Campt**. There is a provision where State laboratories are testing disinfectants.

Senator **Sarbanes**. How many States are doing that?

Mr. **Campt**. I believe something on the order of four or five.

Senator **Sarbanes**. Four, is it not?

Mr. **Campt**. Yes.

Senator **Sarbanes**. Out of 50?

Mr. **Campt**. Yes.

Senator **Sarbanes**. Aside from those four States, what else?

Mr. **Campt**. Now as I understand the question, what could they do if they had questions as to whether the disinfectant worked? Is that the question?

Senator **Sarbanes**. The hospital suspects that this disinfectant does not work. How does the EPA under its current procedures determine whether or not the disinfectant is effective?

Mr. **Campt**. Well, if in fact we were notified that there is a question as to whether the disinfectant works, we could take action to require further testing, as we have done with certain products where questions came up as to whether they were effective against tubercle bacillus, require additional testing, and in some cases require confirmatory testing by independent laboratories.

Senator **Sarbanes**. Do you have the power to remove an ineffective disinfectant from the market?

Mr. **Campt**. Yes.

Senator **Sarbanes**. Have you done that?

Mr. **Campt**. I think there have been disinfectants removed from the market because of ineffectiveness.

Senator **Sarbanes**. When was the last time that was done?

Mr. **Campt**. I don't recall one that has been done in the last year or so, but I do recall in past years there have been products removed from the market because of ineffectiveness.

Senator **Sarbanes**. Well, I'm going to come back to that. I don't want to take too much time. I want to direct a few questions to Dr. Rheinstein and then I'm going to defer to Senator Gore. Then I'll pick up again.

Essentially, Dr. Rheinstein, I want to take you through the same series of questions.

When a manufacturer registers an antiseptic with the FDA, does the registration represent FDA's assurance to the consumer that the antiseptic is safe and effective when used as directed?

Dr. **Rheinstein**. Well, antiseptics aren't registered with FDA in the same way that disinfectants are registered with the Environmental Protection Agency.

As I mentioned earlier, there are basically two routes to market. Either one has a product which is put together from ingredients which are essentially "old friends," products made from ingredients which have been used as antiseptics for many, many years; or the company files what's called a new drug application with FDA, submits data which the Agency reviews.

What is said in the indications section for any of these antiseptics is that they reduce the bacterial count when used according to directions. None of these products eliminate bacteria entirely.

Senator **Sarbanes**. Who tests to make sure that the antiseptic is safe and effective?

Dr. **Rheinstein**. Well, testing antiseptics—in fact, testing of all drug products is essentially conducted by the manufacturer. FDA inspects the testing and in fact we have a division of scientific investigations headed by Dr. Frances Kelsey, who gained fame for her discovery that thalidomide caused the birth defect which in fact it did cause. That group is responsible for both doing inspections themselves and for giving additional assignments to the field to go out to the laboratories and to look at the studies that these laboratories have done.

Senator SARBANES. Senator Gore.

Senator GORE. Let me begin with a couple questions about disinfectants and then turn to antiseptics.

First of all, on disinfectants, Mr. Campt, I referred in my brief opening remarks to the House amendment to FIFRA that requires EPA to establish a monitoring program for disinfectants.

Has EPA begun to explore ways of implementing this provision to establish a monitoring program, including for compliance and enforcement?

Mr. CAMPT. As I indicated in my testimony, Senator, we believe that the approaches that we have outlined in terms of improving our scrutiny on disinfectants really would achieve the same goals that are outlined in Senate bill 2659. And the steps that we are taking and plan to take in the future will accomplish those basic goals.

Senator GORE. Well, regardless of your disagreement on that, have you begun to explore ways of implementing this provision which has already passed the House of Representatives?

Mr. CAMPT. No, we have not made any explicit efforts to do that.

Senator GORE. All right. Now let me ask you about the issue of misleading advertising of disinfectants. I'm going to ask the staff to show you a copy of an advertisement in the August 1986 issue of Infection Control.

This advertisement is for gluteraldehyde, the active ingredient manufactured by Sporeciden, and this advertisement states that it will disinfect scopes safely and completely in just 10 minutes.

Do you want to identify who's joined you at the witness table?

Mr. ABRAMSON. My name is Stanley Abramson and I'm a representative of the Office of General Counsel in the Environmental Protection Agency.

Senator GORE. All right. It states that this active ingredient will disinfect scopes safely and completely in just 10 minutes using a dilute solution.

At the August 7 hearing, we heard testimony that 10 minutes was not long enough, not long enough for TB bacteria on scopes even when using concentrated solutions. It was also noted that EPA has started to reevaluate the 10-minute claim for TB disinfectants.

So my first question is, Is this advertisement inaccurate?

Mr. CAMPT. Senator Gore, Sporeciden is a brand name and there are a number of products that are registered with the brand name Sporeciden I believe. Without commenting specifically on this advertising, I think I would like to be able to associate it with the product involved.

Senator GORE. Well, it says right on it what it is. Sporeciden is attained from gluteraldehyde.

Mr. CAMPT. Yes, but I would question which product is it. Some of the Sporeciden products have recently been subjected to additional data requirements and, quite frankly, I would like to look at the record on this product to see whether or not this product would meet those claims.

Senator GORE. Well, I think the evidence will show that this is an inaccurate advertisement. The Mayo Clinic found that some scopes contained TB bacteria after use and that over 45 minutes was necessary to disinfect them.

Now this same advertisement contains a statement that Sporeciden inactivated the hepatitis B virus. Do you see that? They put a little circle around that and called special attention to that.

However, at our earlier hearing witnesses testified that EPA had not developed a protocol for testing disinfectants for use with hepatitis B or with AIDS for that matter. So is this advertisement illegal from EPA's standpoint?

Mr. CAMPT. I think we've taken the position in a recent policy statement that we issued on claims both for hepatitis B virus and for the AIDS virus that there are not protocols available to determine whether they would be effective and claims that are made for these two organisms without the benefit of registration are in fact inappropriate and our Office of Compliance and Monitoring has taken steps to gain corrective action on that score.

Senator GORE. Have they taken steps against this company or this advertisement?

Mr. CAMPT. I don't know specifically about this product, but certainly we have received information indicating that companies are making claims for hepatitis B virus and AIDS and we have pursued those specific complaints.

Senator GORE. All right. Well, you know, 20,000 deaths a year and here's one of the major journals giving the information out to hospitals saying, "Folks, here's how you fight it. A government study confirms that this will kill hepatitis B." The Government says, "No, it's inaccurate." You have to do something about that. If we're going to organize to fight this problem you have to be more aggressive. You have to get out there and make sure that these claims made by companies are accurate.

Now let me go to the enforcement question in a slightly different area.

Information released at the last hearing documented that one disinfectant manufactured by Huntington Labs was found to be ineffective by EPA in tests in 1981. It was left on the marketplace and then found to be ineffective by the State of Mississippi in 1985. It was left on the market and it was found to be ineffective by the State of Florida this year.

What can be done to see that a product like that, found to be ineffective by the few number of States that have such monitoring, can be removed from the market quickly?

Do you agree that when you have tests showing that a product is ineffective that the EPA ought to prevent it from being marketed so that hospitals don't continue to use it in the mistaken belief that it's going to save lives?

Mr. CAMPT. Yes, Senator, I do agree with that. I think the key is whether the product itself is ineffective by design or by virtue of what is in the product or whether there is something wrong with the quality control.

As you will recall, in my testimony I indicated that one of the things that we are pursuing is the possibility of batch-by-batch or lot-by-lot testing, requiring that, and requiring the maintenance of records and certifications on a lot-by-lot basis. That is one of the things that we are pursuing in our general strategy that will be available after the end of the year.

Senator GORE. Well, does that mean you're going to reopen the lab that you shut down?

Mr. CAMPT. No, it does not.

Senator GORE. Where are you going to test it?

Mr. CAMPT. I think what I indicated is that we would—one of the proposals is that we could require the manufacturer to test on a lot-by-lot basis and certify that lots are effective and maintain records for scrutiny by the Agency on that basis.

Senator GORE. Just again staying with the approach that the company has the responsibility to check itself?

Mr. CAMPT. Well, that is the approach, yes.

Senator SARBANES. Would you concede that that gives a tremendous opening to an irresponsible producer? Many producers are very responsible, but does not the approach you just outlined give a tremendous opening to an irresponsible producer?

Mr. CAMPT. I think that risk probably would be there, but I think that we would have to follow that up with some monitoring and make sure that we aggressively pursue the fact that the studies are conducted and are conducted in accordance with the protocols.

Senator SARBANES. Doesn't it give you pause that your approach differs from the approach taken by every other responsible group that has testified before us? The Public Health Service people, consumer people, State testing people, and the industry itself have all come before us and said that they believe the EPA ought to resume and carry out a valid, effective testing program.

It's not as though there's a difference among the effected parties on this issue. The only difference is in your testimony here today, where you say you can't support Senator Gore's bill.

Mr. CAMPT. I think what we said was that we think that the initiatives that we have underway would achieve—we have the same goals in mind and we think that we could achieve the same goals in terms of the initiatives that we have underway.

I think if you talk about resuming the testing that was conducted at the Beltsville laboratory, I think that there is some misunderstanding about the level of effort in terms of the testing that was going on at the Beltsville laboratory in 1982.

Senator SARBANES. Don't use that scare tactic.

Senator GORE. Our witnesses have all made it very clear that we need to integrate the new knowledge about testing protocols and do it as effectively as it can be done.

What nobody disagrees with, except this administration, is that there ought to be testing by someone other than the companies because, as the chairman points out, if it's left entirely up the companies, then it gives advantage to unscrupulous companies that are willing to cut corners and cheat on the public health in order to make a buck and undercut the responsible companies.

The industry has come in here in favor of this bill. The hospitals are in favor of this bill. The pharmacists, the doctors, all of the health professionals—everybody is in favor of this bill except for a small group of ideologues in this administration that are so blamed reactionary that they don't want the Government to do anything, even when industry, the public health groups, and every single other person who's studied this problem says, "Something has to be done; 20,000 people are dying each year. This is not the total solution to all that problem, of course; but it's a good first step."

Now coming back to the chairman's question, doesn't it give you pause, doesn't it cause you to question the validity of your position when the industry itself comes in here and says, "Please test us, please reactivate this program. We want the Government to test us." Doesn't that cause you to question whether or not you might be just plain flat wrong?

Mr. CAMPT. I would respond to that by saying we receive tests from the industry on health and safety issues—cancer studies, teratology studies, mutagenicity studies—which are done by the industry. And I think I would have the same concern about that.

As I pointed out, I think the approach is to make sure that we monitor and make sure that those tests are done in accordance with existing protocols that we have established.

Senator SARBANES. Well, now, Mr. Campt, you state yourself, in terms of the five primary objectives: "Reproducible efficacy tests. When testing the efficacy of a product, tests of the same material should yield the same results over and over regardless of where the test is conducted or by whom."

Now the testimony before us in August was very clear that the most likely way of achieving that result was to have centralized testing procedures in effect at a lab conducted by the EPA. Then you would have the same personnel using the same procedures in the same location; the likelihood then of reproducible efficacy tests would be at its very highest.

Isn't that correct? Do you disagree with that? You may not want to do that for other reasons, but do you disagree with the view that the greatest likelihood of reproducible efficacy tests would occur if they were being done in the same location by the same personnel using the same protocol, so that you could most likely eliminate divergencies in testing?

Mr. CAMPT. I would agree with that, Senator.

Senator SARBANES. All right.

Senator GORE. Can I pursue this same point? We heard testimony from one of our witnesses, Mr. William Rutala——

Senator SARBANES. Who in fact you cite in your testimony.

Mr. CAMPT. Yes, that's correct.

Senator GORE. You think he's an expert, right?

Mr. CAMPT. That's correct.

Senator GORE. All right. He's conducting a study and in this study he took four disinfectants and took the labels off, removed any identification of what they were, and he sent them to four different companies to have them tested for effectiveness—private companies. Three of the four failed the test and were cited as ineffective.

Then and only then, he disclosed that each of the four samples were sent to the company that manufactured those samples. When they were testing the samples without any identification they failed the company's test. Yet those same disinfectants when they were originally tested for certification by that company passed with flying colors.

Does that give you any pause whatsoever in your belief that the companies themselves can be relied upon to test these products for effectiveness?

Mr. CAMPT. I think that goes to the reproducibility of the test and I think there are issues that I mentioned with respect to test protocols. We need to look at the test protocols more closely and the reproducibility of tests, whether one laboratory can get the same results over and over again as the first laboratory can get.

Senator GORE. Mumbo-jumbo, mumbo-jumbo. Why not check them yourself? Why not seek to verify what the companies have done? You're talking about looking at the protocols, analyzing the protocols, looking at the words, doing all of this, and everything that you can do by looking at a piece of paper prepared by a company. You cannot solve this problem by simply looking at a piece of paper prepared by the company. You already have that piece of paper when they register the product.

The only way you can solve this problem is to check on them to see, to keep them honest, keep all the companies honest, including the ones that are tempted to cut corners and undercut the responsible players.

Senator SARBANES. The fact of the matter is, and the testimony showed it, that your present approach is placing responsible producers at a disadvantage and giving an advantage to irresponsible producers. That's what's happening. Something is wrong with the system when that's the case. There are a lot of responsible producers who are trying to deliver an effective product. To do that is more costly than delivering an ineffective product.

If the system doesn't make any distinctions, then you're advantaging the irresponsible producer. And as we look at it, the only way we see of addressing that problem is for the EPA to have an effective testing program which the irresponsible producers know they won't be able to get through—or they will be taking very high chances in terms of getting through—and the responsible producer is protected and enhanced by the testing program.

Don't you get these reverberations from the industry? Don't you hear that concern from the industry?

Mr. CAMPT. I think probably what we hear from the industry is mixed. I think that that is the unanimous—I don't hear that unanimously from the industry.

Senator SARBANES. Well, it wouldn't be unanimous because the irresponsible ones would not be part of the reverberation. But you're certainly hearing some of that coming from the industry, aren't you?

Mr. CAMPT. I think the testimony that you refer to indicates that there were industry people who supported that position.

Senator GORE. Let me turn to antiseptics and ask you some questions, Dr. Rheinstein.

In January 1978, FDA published a tentative final order for antiseptics in the Federal Register. The final rules would establish conditions for the safety, effectiveness, and labeling of antiseptic products. But they have not been published to date.

What is the status of the final rules and what has caused the 8-year delay?

Dr. RHEINSTEIN. Well, you will be happy to know that we are about to publish a revised proposal. It's not a final rule because it has substantial revisions in it and so we're allowing another chance for comment.

It does include revised testing procedures for over-the-counter, OTC, monographed drugs that will be marketed as antiseptic drug products. It includes our responses to a multitude of data which have been submitted since 1978 which have in fact established the effectiveness of many of our "old friend" ingredients which previously have been in category three.

Senator GORE. Our "old friend" what?

Dr. RHEINSTEIN. Our "old friend" ingredients. As I said earlier, all of the ingredients currently used in antiseptic products are either ingredients that have been in the marketplace for a long, long time—long, long time, meaning 20 years or more—or they are the subject of new drug applications where we have extensive data on the performance of the ingredient.

Senator GORE. Now do you agree that hospitals and doctors ought to be able to rely on the effectiveness of antiseptics as well as disinfectants?

Dr. RHEINSTEIN. It would be hard to argue with that proposition.

Senator GORE. Well, I think it's hard to argue with it, but if you just look at what the administration has done, it would seem that the administration is in a de facto way arguing with it. Now the two cases are different—antiseptics and disinfectants. As everyone knows, disinfectants are used for things like inanimate objects that have micro-organisms whereas antiseptics are used on living tissue. Is that distinction succinctly stated or is there some qualification that we need to be aware of.

Dr. RHEINSTEIN. I think that's accurate.

Senator GORE. All right. Doctors and hospitals ought to be able to rely on them, as you agree, but they can't now. Would you agree with that?

Dr. RHEINSTEIN. That they cannot rely on antiseptics?

Senator GORE. They don't know whether they're effective or not.

Dr. RHEINSTEIN. I'm not sure that's a totally accurate way to state it. We have, for example, an adverse reactions reporting system and one of the things I did in preparation for this morning was to ask our adverse drug reactions group how many reports of no drug effect or infection we've had with any number of these antiseptic products, and it turns out that over the past 5 years—the 5 years that we have in the computer system—there have been a total of seven reports of lack of effectiveness.

Senator GORE. Well, you're aware, are you not, of the expert opinion represented by witnesses at our August 7 hearing that when you have a hospital-caused infection it's extremely rare for anyone to ever find out where that bacteria or other agent came from. They almost never have any idea how the patient got an infection and there's a built-in reluctance to affix the exact cause with any specificity because of the liability problems concerned.

But you would agree that it's very rare to pinpoint the cause of a hospital-based infection, wouldn't you?

Dr. RHEINSTEIN. I'll agree that it's very hard. Actually, more and more hospitals are involving either a doctor assigned full or part time to infection control or even an epidemiologist——

Senator GORE. That's right. We had several of them come here and testify that they cannot do their job because the Government will not do its job. They cannot help their hospitals choose disinfectants and antiseptics that are effective for the job they want them to do because the Government does not give them any help at all in telling them which products are effective and which are ineffective.

In this 1978 order you set up three categories, and the third category was: "Describe conditions for which the available data are insufficient to permit final classification at this time." The first two were "effective" and "ineffective." The third was, "We don't know."

Now how does FDA currently regulate ineffective antiseptics in the marketplace from category 3 where the data is insufficient to permit classification?

Dr. RHEINSTEIN. Products that—or I should say, ingredients that are in category 3 are still permitted in antiseptic products. As I mentioned, these are in fact ingredients which have been in the marketplace for many years and on which the medical community has come to place some degree of credence.

Senator GORE. Is it not possible that a watered down product could exist in the marketplace and FDA could not remove it because ineffectiveness is not illegal so long as the product is in category 3?

Dr. RHEINSTEIN. FDA has been successful at removing products which are unsafe. Let me preface my remarks by saying that.

Senator SARBANES. When you say "unsafe," are you talking about a product which, if used, will actively harm you? Is that correct?

Dr. RHEINSTEIN. That's correct.

Senator SARBANES. Now do you also apply it to a product which it is asserted, if used, will eliminate infection but which does not do it? In other words, let's say the product is just water. So your using it won't harm you in an active sense. But it harms you in the sense that it will not do what it's supposed to do, which is, namely, to kill infection. Do you call that unsafe, too?

Dr. RHEINSTEIN. We would define that as lacking effectiveness. However, if we came across multiple reports that a particular product or a particular ingredient was ineffective, was allowing patients to get infections, we would find a way to act.

Senator SARBANES. But you don't call that unsafe?

Dr. RHEINSTEIN. Well, unsafe in the particular sense that I'm using it, unsafe——

Senator SARBANES. In other words, the product itself would have to infect you in order to be unsafe. If the product is held out as a product that will kill infection but doesn't do it, although it in itself may not actively infect you, then it's not unsafe. Is that correct?

Dr. RHEINSTEIN. Not unsafe in that sense of the word. Let me say that the two ingredients or the two types of ingredients which we removed from the marketplace were not removed because they caused infection. They were removed because they were toxic to the tissues on which they were used. I'm talking about hexachlorophene which was removed from OTC status because it caused neurotoxicity and another set of ingredients which were photosensitizing agents. These agents, when the data came to light, were removed from the marketplace very, very quickly.

Senator **Sarbanes**. Are you familiar with Ms. Larson's testimony in the August hearing? Ms. Larson holds the Nutting Chair in Clinical Nursing at Johns Hopkins University.

Dr. **Rheinstein**. I have seen the testimony. Unfortunately, we received the invitation to today's hearing at quite a late date and so I really have not had an opportunity to review it.

Senator **Sarbanes**. Let me just quote from that testimony. She says, "There has been essentially no direction from any governmental agency regarding acceptable test standards or criteria for choosing appropriate and effective agents." She's talking about skin antisepsis—particularly handwashing, which is the area she's been working in. "To complicate the matter, the Centers for Disease Control which publishes guidelines considered to be the gospel of infection control practice has equivocated in their 1985 guideline for handwashing and hospital environmental control. This guideline gives minimal direction regarding what kinds of soaps or how much should be used. They state that they cannot recommend the use of antiseptics for handwashing by health care personnel because of lack or randomized controlled clinical trials to demonstrate the effectiveness of antiseptic handwashing on decreasing hospital-acquired infection."

Now aren't we right back to this testing problem?

Dr. **Rheinstein**. Well, the Government or at least FDA does not conduct tests nor does it require tests which would establish a so-called drug of choice in any category, including antiseptics.

We do require tests which aim to show whether a product is or is not effective for its labeled indications, in this case to reduce the number of bacteria on the tissue surface that's being washed.

Which ingredient is the most effective in any given hospital may depend on a number of factors. One is simply the predominant bacteria which are present in that particular hospital.

Senator **Sarbanes**. No, no. I'm not trying to identify the one that's most effective. I'm trying to identify those that are ineffective and to find a procedure for excluding them. I'm not asking the FDA to say, "This is the product that should be used." I'm asking the FDA to draw a line and say, "Below this line, these products do not cross the threshold and therefore don't qualify."

Dr. **Rheinstein**. We are working very actively to do that. I think you will be pleased when you see our revision to the tentative final monograph that covers much of these products that are marketed OTC under the OTC monograph program.

In addition, we are working actively in the relevant societies to establish additional test standards which we think will help to meet the same sort of goals for antiseptics that EPA has outlined as goals for disinfectants.

Senator **Gore**. I have two other very brief questions, Mr. Chairman, if we have time.

First, on the question of EPA checking to see whether labels are accurate and setting conditions for labels, let's suppose that a manufacturer changes the concentration of ingredients in an antiseptic and uses the same active ingredient but dilutes it, changes the recommended concentration.

What prevents them from doing that? Can you prevent them from doing that? In other words, at a certain concentration the scientific studies show that it kills hepatitis B—well, that's a bad example, but it kills a particular bacteria. They change the label and they dilute it and recommend that you use just half as much or a tenth as much. OK?

Dr. **Rheinstein**. Well, we actually are involved with one company that did just what you say with respect to an iodine preparation. They have elected to go into the marketplace with a more dilute iodine solution labeled only as a health care personnel handwash. We have asked the company to remove the product from the market.

Senator **Gore**. Well, let me interrupt you here because this is really a different case altogether. This is an iodine solution involving shelf life. They found a way to prolong its shelf life at a lower concentration, but the concentration used was still proven scientifically to be effective at killing the germs in question. It's really a different question, isn't it?

Dr. **Rheinstein**. Well, the product that I'm thinking of, was done because the iodine in the concentration discussed in the monograph, was found to be sufficiently irritating to the skin of health care personnel that they would not use it repeatedly.

Senator **Gore**. But I'm talking about efficacy, where they change the label and dilute a product that's efficacious at a higher concentration, but they dilute it and recommend—and we have some examples—and there's nothing to prevent them from doing that in the current law or regulations. Is that correct?

Dr. **Rheinstein**. That is correct, the bottom line legally is that until the final monograph is published, we cannot remove a product for being out of compliance with the monograph. Nevertheless, when a company reformulates in a way that takes it out of the ingredients or concentration of ingredients which are in our tentative final monograph, we notify the company and attempt to get the company to reformulate or to remove their product from the marketplace.

Senator **Gore**. All right. Would both of you be willing to answer additional questions in writing?

Dr. **Rheinstein**. Yes.

Mr. **Campt**. Certainly.

Senator **Gore**. I would appreciate that. I have a whole series of questions about so-called disposable items for hemodialysis patients and a whole bunch of others, and I would appreciate it if you would answer them in writing. I'm sorry that we're out of time but we are, and I appreciate your efforts again, Mr. Chairman.

Senator **Sarbanes**. I also would say to the witnesses, if they want to review again the testimony of August 7 and submit additional comments related to it, the subcommittee would be happy to receive them.

But, gentlemen, there's a serious problem out there. Every witness has testified to it. There's a general consensus at least on some things that ought to be done to try to deal with that problem, and the only people that are not part of that consensus are the agencies. We may render this situation moot by moving ahead and acting in the Congress on this important question.

Thank you.

The hearing will stand adjourned.

[Whereupon, at 11:10 a.m., the subcommittee adjourned, subject to the call of the Chair.]

[The following letters, containing questions and answers, were subsequently supplied for the record:]

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ROBERT J. TOSTERUD,
DEPUTY DIRECTOR

October 6, 1986

Mr. Douglas D. Campt
Director
Office of Pesticide Programs
Environmental Protection Agency
TS 766C
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Campt:

Will you please answer the following questions, which were submitted by Senator Gore, for the record of the September 25, 1986, hearing before the Subcommittee on Investment, Jobs, and Prices on the subject of hospital disinfectants and antiseptics:

1. As you know, the House adopted an amendment to FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act) that requires EPA to establish a monitoring program for disinfectants.

    * Has EPA begun to explore ways of implementing this provision?

    * What role will the EPA lab in Beltsville, Maryland, play in any future disinfectant monitoring program? Are any other EPA facilities being considered for use in such a monitoring program?

    * What is the estimated cost of a disinfectant monitoring program?

2. Information released at the last hearing documented that one disinfectant, manufactured by Huntington Laboratories, was found to be ineffective in EPA tests in 1981. It was also found to be ineffective by the State of Mississippi in 1985 and by the State of Florida in 1986.

    * What can be done to see that such ineffective products are removed from the marketplace quickly?

    * Does the disinfectant amendment adopted by the House need to be strengthened to give EPA increased enforcement power? If so, how could it be strengthened?

    * Does the amendment provide EPA with the proper authority to stop manufacturers from making false or misleading claims in their advertising?

Mr. Douglas Campt
October 6, 1986
Page Two

3. Dr. Rutala testified that he is nearing completion on the evaluation of the test used to determine disinfectant effectiveness.

    - How long do you think it will be before EPA develops testing standards for disinfectant testing and for effective enforcement purposes?
    - When will a disinfectant monitoring program be in place and functioning?
    - How long will it be before EPA begins an aggressive enforcement program for ineffective disinfectants?

4. Dr. Martha Rhodes testified that she was concerned that a new EPA disinfectant testing program would prohibit the states from having their own programs.

    - What role will states play in the EPA disinfectant monitoring program?
    - Will states be prohibited from conducting their own tests for disinfectant effectiveness in the future?

I would appreciate having your response at your earliest convenience.

Again, thank you very much for participating in the hearing and for your very useful testimony.

Sincerely,

Paul Sarbanes
U.S.S.

PS:bbt

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

DEC 5 [illegible]

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Honorable Paul S. Sarbanes
United States Senate
Washington, D.C. 20510

Dear Senator Sarbanes:

Thank you for your letter of October 6, 1986, in which you set forth several questions posed by Senator Gore for the record of the September 25, 1986, hearing before the Subcommittee on Investment, Jobs, and Prices on the subject of hospital disinfectants and antiseptics.

Those questions and the Agency's answers are enclosed, along with our responses to certain additional questions which were posed during the hearing. These responses were delayed by difficulties encountered in obtaining a copy of the transcript.

I hope the information provided is helpful. Again, I want to thank you for the opportunity to discuss this important subject with the Subcommittee. I am sorry I was unable to attend personally, but I am confident in Mr. Campt's competence to address any of the Agency's pesticide programs. If you have any further questions, please let me know.

Sincerely yours,

JAMoore
John A. Moore
Assistant Administrator
for Pesticides
and Toxic Substances

Enclosure

QUESTIONS AND ANSWERS RE: DISINFECTANTS PROGRAM

1. As you know, the House adopted an amendment to FIFRA that requires EPA to establish a monitoring program for disinfectants.

   Has EPA begun to explore ways of implementing this provision?

   What role will the EPA lab in Beltsville, Maryland, play in any future disinfectant monitoring program? Are any other EPA facilities being considered for use in such a monitoring Program?

   What is the estimated cost of a disinfectant monitoring program?

ANSWER:

As you know, the FIFRA legislation was not passed prior to adjournment in October. However, as Mr. Campt explained in his testimony before the Subcommittee, the Agency has been scrutinizing its disinfectants program and has come up with five objectives for the improvement of the program. One of those five points is "Quality Control." To assist the Agency in developing a strategy to attain these five objectives, I have retained Dr. William Miller, an expert in the field of microbiology, to provide advice to the Agency on approaches for improving this program. We expect to have developed a strategy by early 1987 and will provide it to the Subcommittee at that time. Until we have a better idea of the type of monitoring which would be necessary, it is impossible to estimate costs.

2. Information released at the last hearing documented that one disinfectant, manufactured by Huntington Laboratories, was found to be ineffective in EPA tests in 1981. It was also found to be ineffective by the State of Mississippi in 1985 and by the State of Florida in 1986.

   What can be done to see that such ineffective products are removed from the marketplace quickly?

   Does the disinfectant amendment adopted by the House need to be strengthened to give EPA increased enforcement power? If so, how could it be strengthened?

Does the amendment provide EPA with the proper authority to stop manufacturers from making false or misleading claims in their advertising?

ANSWER:

EPA possesses authority under FIFRA section 6 to cancel the registration of a pesticide if, using the cancellation procedures set out in section 6, EPA finds that the risks caused by use of a pesticide outweigh the benefits of use. And, if use of a pesticide is found to pose an imminent hazard, the registration can be suspended while a cancellation hearing is held. Thus, the law already provides authority for removal from the market of a product whose lack of efficacy itself poses a health risk. Using this authority can require large amounts of Agency resources, however, because of the relatively cumbersome process the law mandates; the Agency thus has to decide whether cancelling these products is the best use of the resources that would be required.

Congress could make it less costly for EPA to remove ineffective disinfectants from the market by enacting legislation lessening the procedural protections afforded by current law to registrants whose products fail to meet published efficacy criteria.

FIFRA section 13 provides that the Agency may issue a "stop sale, use, or removal" order and may seize pesticide products which are in violation of FIFRA. Further, under section 16(c), a court may enjoin a registrant from violating the Act.

The 1986 House bill's disinfectant provision did not purport to deal with advertising claims. EPA believes that it has considerable authority to regulate false or misleading advertising of registered pesticides under FIFRA section 12(a)(1)(B), although this position has not yet been confirmed by court decisions.

3. Dr. Rutala testified that he is nearing completion on the evaluation of the test used to determine disinfectant effectiveness.

   How long do you think it will be before EPA develops testing standards for disinfectant testing and for effective enforcement purposes?

   When will a disinfectant monitoring program be in place and functioning?

   How long will it be before EPA begins an aggressive enforcement program for ineffective disinfectants?

ANSWER:

Testing standards and performance standards have been published, adopted, and used as registration and enforcement criteria for almost 20 years. There have been allegations in recent years by some members of the antimicrobial pesticide industry that failures of products when tested by certain AOAC standard methods are due to deficiencies in the methods, rather than in their products or their testing programs. This concept has been widely promoted by the industry. To date, scientific evidence is not available which documents variability in test results or that failing test results are due to deficient test procedures, rather than to other aspects of the testing program.

The Agency has contracted with Dr. Rutala to conduct studies to evaluate the AOAC Use Dilution Test (UDT), one of the several test methods used for testing antimicrobial pesticides. A preliminary report of the initial phase of his studies on this method is expected in early 1987. The report is expected to address several minor procedural clarifications and improvements in the method. Using these recommendations, the Agency intends to make the UDT as unambiguous as practicable.

The AOAC Tuberculocidal Activity Method is a test protocol with which we have encountered problems with respect to gluteraldehyde-based products. As Mr. Campt stated in his testimony, the Agency has already taken steps to correct that problem by the adoption of a new policy on tuberculocidal efficacy testing. The Agency expects to initiate collaborative studies, through the AOAC, on the new quantitative tuberculocidal testing procedure. This procedure was developed as an alternative to the AOAC Tuberculocidal Activity Method, primarily for glutaraldehyde-based products. This group of products requires different use conditions for efficacy than those specified in the AOAC method, and therefore, the new, more appropriate methodology was developed to assay the specific use conditions (temperature and exposure time) needed for glutaraldehyde tuberculocidal efficacy.

At this time, the Agency considers the existing standard AOAC test procedures to be valid test criteria for registration and enforcement purposes. However, the Agency is developing other strategies for a comprehensive upgrading of the testing program for antimicrobial pesticides that will address not only methodology, but also the other obvious deficiencies in the industry-based efficacy testing program for these products.

As stated above, the Agency has not yet developed its strategy for improvement of monitoring and enforcement.

4. Dr. Martha Rhodes testified that she was concerned that a new EPA disinfectant testing program would prohibit the states from having their own programs.

   What role will states play in the EPA disinfectant monitoring program?

   Will states be prohibited from conducting their own tests for disinfectant effectiveness?

ANSWER:

Again, let me emphasize, quality control is one of our top priorities in the development of a strategy for the disinfectants program. The states have always played an important role in enforcement of pesticide laws and regulations; the Agency relies on their valuable support; and I see no reason to change that relationship.

ADDITIONAL QUESTIONS FROM THE HEARING, SEPTEMBER 25, 1986

QUESTION:

How many audits has the Agency done during the past year to address whether a test was actually done and that the data submitted were accurate?

ANSWER:

Attached is a copy of a computer print out listing the antimicrobial efficacy studies audited from March 1985 to September 9, 1986.

QUESTION:

When was the last time a disinfectant was removed from the market because of ineffectiveness?

ANSWER:

A comprehensive examination of the cancellation records and reasons for cancellation would be extremely time-consuming; however, I am not aware of any pesticide product of any kind being cancelled because of ineffectiveness since 1980.

QUESTION:

What action has been taken in response to the Sporicidin advertisement which claims to inactivate the hepatitis B virus?

ANSWER:

As shown by the attached letter of September 12, 1986, the Agency has advised the Sporicidin Company that such claims of efficacy are in violation of FIFRA section 12(a)(1)(B), and subject to further enforcement action. Since that letter was written, officials of our Office of Compliance Monitoring have met with representatives of Sporicidin. Sporicidin has claimed that the First Amendment protects their right to cite the CDC study. The Agency's position is that the ad is in violation of 40 CFR 162.10(a)(5)(vii). If they continue to use the CDC study in their advertising, the Agency will have to litigate.

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DEPUTY DIRECTOR

October 6, 1986

Dr. Peter H. Rheinstein
Office of Drug Standards
Center for Drugs and Biologics
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Rheinstein:

Will you please answer the following questions, which were submitted by Senator Gore, for the record of the September 25, 1986, hearing before the Subcommittee on Investment, Jobs, and Prices on the subject of hospital disinfectants and antiseptics:

1. In disinfectants, one product manufactured by Huntington Laboratories failed effectiveness tests by EPA in 1981, the State of Mississippi in 1985, and the State of Florida in 1986. Yet, the product was not removed from the market place.

   * What procedures does FDA use to keep ineffective antiseptics, similar to this disinfectant example, out of the marketplace?

   * In North Carolina, the testing program uncovered disinfectants that were contaminated with bacteria before the product was used in the marketplace. On the other hand, apparently only contaminated antiseptics are found after the patients become infected. Does FDA have any programs to monitor antiseptics before they reach the marketplace?

   * It appears that FDA relies on marketplace failure of products as a means of regulating ineffective antiseptics, thereby making the hospital patients the test animals. Does FDA have any other means of regulating ineffective antiseptics?

2. Many hospital devices that cannot be sterilized using heat and steam are reused and chemicals are used to clean them. One such device which is reused is the hemodialyzers. Almost 50 percent of disposable hemodialyzers are reused. Yet, FDA has no guidelines for the effective use of antiseptics in decontaminating instruments from AIDS virus.

- * How safe and virus-free are disposable medical devices that are cleaned and reused? What scientific evidence do you have to support your answer?
- * What scientific data are there that antiseptics in the market will destroy AIDS virus in reused hemodialyzers?
- * When will FDA develop a protocol for antiseptics to be used on AIDS virus?

3. FDA has not been able to formulate final orders to establish conditions for the safety, effectiveness, and labeling of antiseptics.

    - * Would another blue ribbon panel of non-FDA experts in the field of antiseptics charged with recommending final orders be a step in the right direction?
    - * Would legislation mandating a time limit for establishing final orders be complied with by the agency?

4. Does the agency have any plans to develop a program to test the effectiveness of antiseptics in the marketplace?

    Does the agency plan to rely on the marketplace to determine the effectiveness of antiseptics in the future or will hospital patients determine with their health and lives if an antiseptic is effective or not?

I would appreciate having your response at your earliest convenience.

Again, thank you very much for participating in the hearing and for your very useful testimony.

Sincerely,

Paul Sarbanes

Paul Sarbanes
U.S.S.

PS:bbt

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
Rockville MD 20857

July 30, 1987

The Honorable Paul S. Sarbanes
United States Senate
Washington, D.C. 20510

Dear Senator Sarbanes:

This is in response to your request for answers to additional questions from Senator Gore for the record of the September 25, 1986 hearing before the Subcommittee on Investment, Jobs, and Prices on the subject of hospital disinfectants and antiseptics.

Enclosed are the responses to the questions listed in your October 6, 1986 letter.

I hope this information is helpful in clarifying the role of the Food and Drug Administration (FDA) in carrying out our mandate to assure the safety and effectiveness of the products we are responsible for regulating. If there is any way I can be of further assistance, please do not hesitate to contact me.

Sincerely yours,

Hugh C. Cannon
Associate Commissioner
for Legislative Affairs

Enclosure
Reponse to Questions

Question 1: In disinfectants, one product manufactured by Huntington Laboratories failed effectiveness tests by EPA in 1981, the State of Mississippi in 1985, and the State of Florida in 1986. Yet, the product was not removed from the market place.

- What procedures does FDA use to keep ineffective antiseptics, similar to this disinfectant example, out of the marketplace?

- In North Carolina, the testing program uncovered disinfectants that were contaminated with bacteria before the product was used in the marketplace. On the other hand, apparently only contaminated antiseptics are found after the patients become infected. Does FDA have any programs to monitor antiseptics before they reach the marketplace?

- It appears that FDA relies on marketplace failure of products as a means of regulating ineffective antiseptics, thereby making the hospital patients the test animals. Does FDA have any other means of regulating ineffective antiseptics?

Response

It is important at the outset to distinguish between antiseptics, which are formulations for use on skin and other living tissue to arrest or prevent the growth of microorganisms, and disinfectants, which are employed to destroy harmful bacteria or viruses present on environmental surfaces, including medical equipment. Antiseptics are regulated by the FDA under the same provisions used for drugs. Disinfectants are regulated by the Environmental Protection Agency (EPA), except when they are used on medical devices. When antimicrobial agents are labeled, promoted or otherwise intended for use on a medical device, they are considered to be medical devices themselves under the definition for medical device in section 201(h) of the Federal Food, Drug, and Cosmetic Act (FDC) Act, if it is a "component, part or accessory" to a medical device, and as such are regulated for those purposes by the FDA. The agents used on medical devices will be discussed in answer to question #2.

FDA's Regulatory Procedures for Antiseptics

FDA regulates and monitors the safety and effectiveness of antiseptics, both premarket and postmarket, in the same manner as it does for all drugs:

(a) Under the "new" drug provisions of the FDC Act, section 505, includes a comprehensive premarket application process as well as postmarketing inspection and sampling procedures and adverse reaction reporting requirements. Virtually all prescription drugs that have been marketed for the first time since 1938, as well as those over-the-counter drugs containing ingredients with relatively brief, little or no marketing history are considered as "new" under the terms of the FDC Act. All "new" drug applications (NDAs) submitted by the sponsors of these drugs, must describe how the effectiveness of these drugs was established through well-controlled scientific studies and must provide information concerning the sponsor's ability to manufacture the drug in accordance with the current Good Manufacturing Practice Regulations (GMP) 21 CFR Parts 210 and 211-229). The FDA extensively reviews the data and determines whether the application is approvable. Until approved, a "new" drug including an antiseptic cannot be marketed.

(b) The Over-The-Counter (OTC) Drug Monograph review procedures cover OTC drugs that are not in the "new" designation described above. The OTC review evolved out of the 1962 Drug Amendments to the FDC Act, which requires that all drugs, both prescription and nonprescription (OTC) must demonstrate that they are effective in addition to previous requirements of safety. With over 300,000 drugs on the market in the OTC classification, it was decided that requiring each product to go through a "new" drug application would be an impossible regulatory task, and would clog the channels needed to continue current NDA reviews. Since there are only about 500 active ingredients in the 300,000 products, it was decided to group the OTC drugs into categories by ingredients and develop a "monograph" for each category. A monograph lists permissible ingredients, their permissible amounts and labeling claims. The procedure is the same as for regulations, allowing for public comment. A product in compliance with a final monograph can remain on the market without having to file a "new" drug application. A product not in compliance would have to conform or obtain marketing approval through a "new" drug application. Seventeen panels of experts, mostly from outside the Government, and within the speciality of the category under review, were formed to review all data and make recommendations. With the first phase or panel review phase completed, the Agency development phase is currently underway. Since many of the antiseptics in use today were in existence prior to 1962, they fall within the OTC review process. The current status of the OTC Monograph for Topical Antimicrobial Products is discussed in reply to question 3.

(c) The United States Pharmacopeia (USP), and the National Formulary (NF), are recognized as official compendia and are referenced in various statutes as a basis for determining the strength, quality, purity, packaging and labeling of drugs and related articles. Section 501 of the FDC Act states that if a manufacturer makes a product named in the USP or the NF the product must comply with those standards. These are chemical specifications only and do not address the efficacy against specific target organisms. The effort to establish efficacy standards is addressed under the OTC monograph commentary above.

(d) FDA compliance mechanisms include inspection and testing programs as well as legal sanctions if necessary. The FDA conducts periodic inspections of all manufacturers of drug products. The law requires inspections at least once in every two-year period to determine the adequacy of the manufacturer's compliance with GMP regulations. Each manufacturer is required to register with FDA and list their products. The FDA does test products for conformance to quality characteristics. From time-to-time we test products for conformance to the USP, NF, and OTC Monographs where they exist, NDAs or manufacturer's "release" specifications. The FDC Act provides for means to keep noncompliant products from the market including seizure and injunction. FDA may also request manufacturers to recall noncompliant products. Criminal penalties are provided as well.

Historically, antiseptics have been shown to be generally safe and effective and have not demanded constant routine sampling surveillance. When there have been rare isolated incidents of poor product performance, the FDA has responded very quickly to remedy the situation. Isolated reports of problems with antiseptics are investigated through direct assignments to our field offices for either market sampling of the suspect product or inspection and sampling at the manufacturer's plant. We have recently conducted an inspectional survey of povidone-iodine solutions and the data is currently being tabulated.

The current Good Manufacturing Procedures which all manufacturers of drugs and antiseptics are required to employ, require that manufacturers establish and follow very specific control procedures to conduct sampling and testing of in-process materials and products to assure identity, strength, quality and purity of the products as well as controls for microbiological contamination. Failure to adhere to the GMPs can result in more frequent random testing by FDA's compliance division and/or enforcement of the compliance mechanisms referred to in section (d) above.

Question 2: Many hospital devices that cannot be sterilized using heat and steam are reused and chemicals are used to clean them. One such device which is reused is the hemodialyzers. Almost 50 percent of disposable hemodialyzers are reused. Yet, FDA has no guidelines for the effective use of antiseptics in decontaminating instruments from AIDS virus.

* How safe and virus-free are disposable medical devices that are cleaned and reused? What scientific evidence do you have to support your answer?

* What scientific data are there that antiseptics in the market will destroy AIDS virus in reused hemodialyzers?

* When will FDA develop a protocol for antiseptics to be used on AIDS virus?

Response

FDA's Authority Over Disinfectants

The scope of FDA's regulatory authority, as it relates to chemical disinfectants used in conjunction with medical devices, encompasses two main areas: (1) the manufacture of sterile devices; and (2) the safety and effectiveness of disinfectants used in reprocessing devices by medical facilities.

In the first instance, FDA has the responsibility of ensuring that medical devices labeled as sterile are manufactured in accordance with Good Manufacturing Practices (GMPs) (21 CFR 820). (This applies to original manufacturers as well as entities--known as contract sterilizers--who sterilize finished medical devices for the manufacturer.) Specific criteria developed by the Agency, are used by FDA inspectors during biennial site visits to manufacturing plants to check on the viability and reliability of sterilization methodologies used by manufacturers (such as liquid chemical sterilants, ethylene oxide, irradiation and steam). They also review firms' validation of these processes and their packaging techniques designed to preserve the integrity of the sterilized product. If GMP problems are identified, Agency inspections are conducted on more frequent intervals.

Secondly, FDA bears the responsibility for reviewing disinfectants used by medical personnel for reprocessing and reuse of devices already in commercial distribution. It should be emphasized that FDA's jurisdiction, however, does not extend to the actual practice of reprocessing by medical facilities which engage in such activities solely in connection with treatment of their own patients. The basis for this restriction is that such practice does not constitute an interstate or commercial transaction and generally falls within the realm of medical practice. In fact, an FDA compliance policy guide on reuse of disposable medical devices issued in 1981 is still in effect today. It essentially concludes that an institution or practitioner reusing a disposable device is responsible for assuring its continued cleanliness and sterility, that reprocessing does not adversely affect the device's physical properties, and that the reprocessed device can continue to function safely and effectively.

Antimicrobial agents (a generic term that includes disinfectants, sterilants and germicidal materials) that are labeled for use on medical devices are subject to FDA regulation under authority derived from the 1976 Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act. In this regard, FDA requires manufacturers of antimicrobial agents with specific medical claims to submit what is known as a premarket notification (or 510(k)) prior to commercial marketing. The purpose of this requirement is to enable the FDA to review relevant information in order to judge the comparability of "new" disinfectants in terms of their safety and effectiveness to other agents which were on the market prior to enactment of the 1976 device law.

In reviewing new agents, FDA examines a number of performance-related factors, including microbicidal effect, toxicity, residue levels and the effects of the disinfectant on device materials. To date, FDA has granted marketing clearance for 10 chemical disinfectants, based largely on determinations of equivalence to formaldehyde, a general purpose disinfectant for which there is a substantial body of scientific evidence supporting the effective use of this material over the last two decades.

It should be underscored that FDA's regulatory controls over these ten disinfectants apply only when claims are being made regarding use of a disinfectant in conjunction with a medical device, thereby making them device accessories. Many of these same materials are also used for general, nondevice disinfection (e.g., for hard surfaces). In all cases, manufacturers must register with and secure a license from the Environmental Protection Agency (EPA), which under the Federal Insecticide, Fungicide, and Rodenticide Act, reviews general purpose disinfectants for effectiveness.

To avoid inconsistencies and redundancies in the data requirements manufacturers must meet to obtain marketing approval by EPA or FDA, we are formalizing the procedures the Agency has used thus far in evaluating new disinfectants. In developing our guidance, we have drawn upon the expertise that resides in both EPA and the Centers for Disease Control (CDC). By so doing, we ensure that the guidance is comprehensive, is in keeping with the current state of knowledge, and that it prescribes criteria that, if met, satisfy the premarket requirements of either regulatory agency or both.

FDA Guidance on Disinfectants for HIV

In the question, you expressed concern about the lack of FDA guidance on the effectiveness of disinfectants in preventing the transmission of the HIV or "AIDS virus." To date, there is no epidemiological evidence to suggest that currently-available disinfectants are ineffective in preventing the transmission of HIV or that actual cases of HIV can be traced to the inability of current disinfection modes to inactivate the virus. In addition, for disinfectants marketed after 1976, manufacturers had to prove that their agents were as bactericidal as formaldehyde and performed according to the labeled claims. It would, of course, be extremely hazardous to require each manufacturer to test against pathogens such as HIV, so testing is generally conducted against organisms that are not disease-producing but are extremely resistant to chemical germicides. Studies have shown that an ability to kill the resistant nonpathogen demonstrates an ability to kill less resistant pathogens. For these reasons, FDA has not singled out HIV for special testing or review as part of premarket evaluations of new disinfectants. FDA staff are continually reviewing the latest scientific evidence from CDC and the clinical and scientific communities with respect to the issues of medical devices, disinfectants, sterilization, and device reuse in order to make necessary changes in our regulatory practices if the need is indicated.

This is not to suggest that no guidance exists respecting disinfection for HIV. In a November 15, 1985 Morbidity and Mortality Weekly Report (MMWR), CDC published "Recommendations for Preventing Transmission of HIV in the Workplace." In that MMWR, CDC noted that studies done to date overwhelmingly show that high-level and intermediate-level disinfection is effective against HIV, and thus no change in disinfection practices in medical facilities is warranted. FDA staff are cooperating with CDC and health professional groups in updating and promoting these recommendations.

Hemodialyzers and HIV

In your question, you singled out hemodialyzers as one medical device about which there may be concern regarding HIV transmission given the high frequency of reprocessing and reuse. Available data show that over 60 percent of U.S. facilities performing renal dialysis today reprocess and reuse dialyzers, compared to an estimated 16 percent in the late 1970's. There are several reasons for this dramatic increase, not the least of which are the favorable results determined by a number of conferences devoted to examining the safety of dialyzer reuse and published research studies, including the latest technical review in 1986 by the Public Health Service (PHS) Office of Health Technology Assessment.

In discussing what evidence exists pertaining to whether available disinfectants are capable of destroying the AIDS virus or preventing its spread among dialysis patients, one CDC study should be highlighted. In 1985, the CDC published the findings of a study it performed in cooperation with a number of dialysis facilities to determine the prevalence of the AIDS disease among their patients. In a June 13, 1985 Morbidity and Mortality Weekly Report, the CDC advised that dialysis patients who have HIV infection can be dialyzed safely in the same manner as other patients without fear of transmitting HIV infection to dialysis personnel or patients not infected with HIV. In that same MMWR article, CDC reemphasized the need for adherence to routine infection control precautions by dialysis center staff. These procedures include specific disinfection methods for dialysis machines; allowable reuse of dialyzers but strict avoidance of using an individual reprocessed dialyzer on more than one patient; rigorous application of blood and barrier techniques commonly employed in dialysis facilities, such as use of gloves and gowns and handwashing by patients and medical personnel; and precautions against needlesticks.

The critical factor in reusing dialyzers--whether it involves the prevention of HIV or bacterial contamination--is the adherence to accepted reprocessing protocols. This of course includes the selection of disinfectants based on the particular type of dialyzer used and the proper use of such disinfectants. CDC has concluded that, "[C]chemical germicides used for disinfection and sterilization of devices in the dialysis center are effective" against transmission of HIV.

There are several disinfectants which FDA has permitted to be marketed expressly for use in reprocessing of dialyzers, but formaldehyde appears to be the germicide of choice. A CDC study found that in 1984, 85 percent of all dialysis centers used formaldehyde, either to control bacterial contamination in the dialysis fluid pathways or in reprocessing dialyzers or both. It should be noted that the guidelines issued last year by the Association for the Advancement of Medical Instrumentation (AAMI) dealing with dialyzer reuse referenced the use of formaldehyde. The guides prescribed the critical factors for the safe and effective use of this agent--that is, concentration, contact time and temperature.

It is worth noting that the AAMI guidelines formed the basis for the recently-proposed changes by the Health Care Financing Administration in its End-Stage Renal Disease (Medicare) regulations. If adopted later this year, dialysis facilities wishing to maintain their eligibility for Federal reimbursement must comply with these reprocessing and reuse protocols.

Question 3: FDA has not been able to formulate final orders to establish conditions for the safety, effectiveness, and labeling of antiseptics.

- Would another blue ribbon panel of non-FDA experts in the field of antiseptics charged with recommending final orders be a step in the right directions?
- Would legislation mandating a time limit for establishing final orders be complied with by the agency?

Response

Status of the Monograph for OTC Topical Antimicrobial Products

The OTC monograph review process has been described as essentially a three-phased project. The first was the panel of experts review phase which has been completed. The second is the Agency review which is well on its way toward completion, and the final phase of compliance with the final monographs will, of course, begin once the final regulations have been published.

Initial proposed regulations for the Antimicrobial I Monograph, which includes personal hand scrubs, bar soaps, skin antiseptics, and numerous similar products including those used in hospitals, were first published in 1978. Currently, proposed amended tentative final regulations in this area have been written and are under review within the Agency. It is hopeful they can be approved for publication before the end of 1987. Procedures then call for a 60 day comment period and a one year period when new data can be submitted by manufacturers and the public for review in order to be included in the final monograph. Once the Agency has had the opportunity to review this further input, publication of final regulations can be expected.

In reply to your question of whether another panel of experts in this area would expedite the work currently being done by the Agency, it is our firm opinion that it would not. Outside panels cannot publish regulations or necessarily be aware of all the legal consequences of all decisions that must be made in this area. These experts which hold jobs in their own field, cannot involve themselves in the many years of detailed review that have been conducted by Agency personnel in the phase of work that can only be done by the Agency. The planned timetable stated above has been necessitated by the complexity of the undertaking and is one which seeks to balance the demand for final regulations in this area with responsible decisionmaking.

The fact that the monograph is not completed has not stopped activity in this area. If an ingredient on the market is suspected of being dangerous either because of toxicity or lack of efficacy, the Agency can step outside of its routine to evaluate the situation as it did when it removed hexachlorophene from the over-the-counter market and required prescriptions for its use and when it removed tribromsalan from the market completely.

The Agency development phase of the OTC monograph review process has taken considerably longer than was initially anticipated since it has proven to be much more complex than originally envisioned. The staff has run into many scientific difficulties in the process, data is complex to review, new data is being submitted all the time and scientific data is never black and white, the shades of possible interpretation must also be weighed.

Question 4: Does the agency have any plans to develop a program to test the effectiveness of antiseptics in the marketplace?

Does the agency plan to rely on the marketplace to determine the effectiveness of antiseptics in the future or will hospital patients determine with their health and lives if an antiseptic is effective or not?

Response

To reply to question number four, it is important to distinguish between Clinical Testing to establish the efficacy of a product and Chemical Analysis Testing to measure the amount of ingredients in each product.

Clinical Testing to prove a product will fulfill a sponsor's claims is the responsibility of the manufacturer desiring to market a drug in the case of a new drug application (NDA). For over-the-counter products the monograph system is in various stages of development depending on the category of drug. FDA does not see the need to develop testing facilities of our own for this purpose.

Chemical Analysis Testing against an established standard such as the U.S. Pharmacopeia, National Formulary, OTC monographs, New Drug Applications or manufacturer's "release" standards, is already a part of FDA's established compliance procedures. These tests would assure that a compound requiring between 90 to 110 percent of a certain ingredient, does in fact contain that quantity of that ingredient. This differs, of course, from the type of clinical testing to prove a product is effective against a particular microorganism.

As noted in our response to question 1, FDA compliance mechanisms include testing programs in which we test products for conformance to the USP, NF and OTC Monographs where they exist, NDAs or manufacturer's "release" specifications.

For antiseptics, as well as for all other drugs, our testing does not repeat the basic clinical testing, it is chemical analysis testing. This chemical analysis testing assures that products in the marketplace are identical to those originally tested for efficacy.

Repeated clinical testing would add little in the way of assurance, but a great deal in the way of cost.

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